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Gelatin Based Skin Regenerative Template: Market Research and Product Analysis

by

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A Management project presented in part consideration for the degree of "Title of MBA Degree".

Abstract

Skin regeneration and wound management in the Bio-Pharma industry has been an area with constant research and new product development. The range of products includes foams, sheets, sprays, powders, hydrocolloids and gels. Majority of these products that exist in the market are collagen based products. However, using collagen products is very expensive and could also have long term risks on patient's health. Furthermore, they do not regenerate the skin to its original shape and texture and thus leave a scar post treatment.

As an alternative to these collagen based products, a more cost effective gelatin based skin regenerative product is being developed using cutting edge technology. The new product also promises complete healing of the burnt surface without retaining any marks or scars on the patient.

This research explores the newly developed Skin regenerative product at a macro level, with operations, marketing and cost objectives included. The market analysis includes specifics to the Indian market and the focus is mainly on the Wound and Skin management of the Bio-Pharma market. The different stages of the product life cycle and phases of clinical trials are analysed. Potential market segments and niches for the new product are identified and by using competitive benchmarks, the product is analysed for customer applications.

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Chapter 1: Introduction

1.1. Background

Research Councils UK (RCUK) has announced £12 million of funding for collaborations between British universities and institutions in India, China, and the UK. Three large-scale UK-India collaborations have been agreed as part of this scheme, and will be jointly funded by the RCUK and the Department of Science and Technology (DST), India. As a part of this major project by the two governments a two-year grant of £1.5 million has been made to the University of Nottingham, the Indian Institute of Management, Bangalore, and the Indian Institute of Technology, Kanpur. The three partners aim to create a step-change in collaborative innovation in target identification, drug discovery, drug delivery and manufacturing. They will build on existing collaborations with the goal of producing clinical and commercial benefits from patent protected research (BioSpectrum, 2009).

As a part of this initiative, a team from IIT Kanpur is working on several ground breaking researches under the "Science Bridge Project" banner. There are several Bio-Pharma products that are being developed under lab conditions in collaboration with University of Nottingham. The primary focus of this research is to explore the market and product that is being developed for Skin Regeneration & Wound Management.

1.2. Aims & Objectives

There are several players in the market who specialize in the wound and skin care management, therefore, the primary focus of the research is to study the market potential for a new product entry of a skin regeneration template. This research is focused mainly on the Indian market although at the macro level the science bridge project is a tri-nation (UK, China and India) initiative. The research aims at understanding the Indian regulations, government policies and market potential for the new Bio-Pharma product. By understanding the product life cycle in a Bio-Pharma industry in India, the report aims at understanding the current position of the product in the life cycle, highlighting the challenges and providing suitable recommendations for a smooth role out into the market.

The new skin regenerative graft template is one of its kind, it is gelatin based unlike its competitors' products that are all collagen based. The research aims at analysing the competitors' products, understanding the new product at a business level and critically evaluating it. Since the target market initially is in a developing country like India, the research aims at analysing the appropriate pricing for the product.

1.3. Structure of the Report

The report is structured in an analytical framework with a mix of both qualitative and quantitative data. Chapter 2 is an overview of previous literature on new product introduction in the pharmaceutical sector. The main topics of discussion are pricing of a new product and exploring the key aspects of supply chain in Bio-pharmaceutical (Bio-Pharma) industry. This section also explores tissue engineering at a macro level and more specifically the research

done till date on burn and skin re-engineering. Finally, the section concludes with the applied research done so far on treating burns (2^{nd} and 3^{rd} degree) and deep wounds.

After a brief description on the methodology in Chapter 3, the report flows into the quantitative aspects of the research. Chapter 4 begins with the analysis of the pharmaceutical market and exploring why there is a shift of focus to India? The research then narrows down to Biotechnology and Bio-Pharma markets in UK, China and India. A detailed analysis on the regulatory environment in India is explored to understand the policies of Indian government in the Bio-Pharma sector and also the funding opportunities. The market for Clinical trials in India is carefully analysed to be prepared for any challenges and to mitigate risks for the new skin regenerative product.

Before starting the analysis of the new product, a background on the layers of skin, burns and wound management is explained and the characteristics of the existing skin regenerative products in the market and their drawbacks are tabulated. Chapter 5 is a detailed description of the new skin regenerative product. This section has all the relevant data gathered during the interviews and field visits to hospitals, it mainly involves the analysis of the qualitative data. Based on the financial data gathered, a pricing for the new product is extrapolated. Chapter 6 contains discussion on empirical evidence as against the literature review on areas such as pricing, product life cycle and external factors that influence decision making. Chapter 7 contains the summary of the research for the new gelatin based skin regenerative graft with conclusion and recommendations. The report concludes by highlighting the areas for further research.

Chapter 2: Literature Review

2.1. New Product Introduction

In this context, 'product' means tangible products i.e. goods. The term 'goods' refers to physical, tangible products that can be owned, traded, and distributed to different places at different times without changing their identity. However, a product in a modern world can also be something very intangible such as a piece of software, a piece of knowledge or an algorithm or a formula (Saaksvuori, A, 2008). New Product Introduction could be defined as the launch process of a new product, which starts from the product idea and ends with the arrival of the product on the market (Immonen, A, 2008).

The new product discussed in this research is a Bio-Pharmaceutical based product. The different phases in product life cycle are analyzed in chapters to follow. One of the strong arguments of the new product is the price competitiveness. Thus this section explores the literature on product pricing.

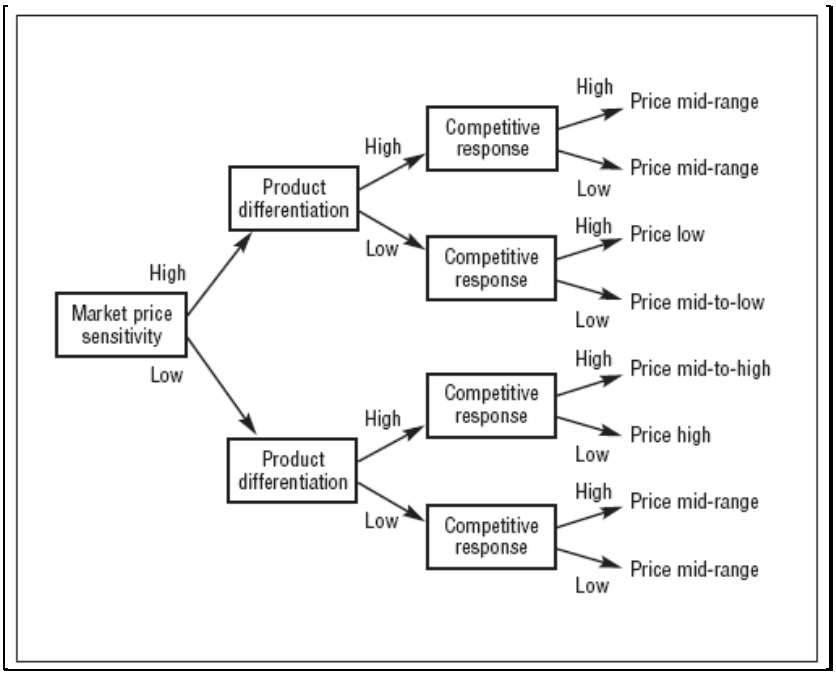

Figure 1: Considerations in new product pricing.
Source: The Product Manager's Handbook

There are several things that need to be considered to estimate the target price of a product. Some of such factors are possibility of competitive attack, the price sensitivity of the market and the degree of competitive differentiation. The figure 1 adapted from 'The complete product management resource' (Gorchels, L, 2000) is a tree diagram with the considerations in the new-product pricing.

For example, the product would be highly differentiated if the target customers are not price sensitive, and competitive response is not expected, it is conceivable to charge a relatively high price. However, low price will be necessary if the price sensitivity is high, product differentiation low and competition is heavy.

The book states that a rough business analysis will have been prepared prior to new-product proposal and a continually evaluated to make it more definitive as new information becomes available. Ideally it would be when significant milestones are achieved. The author argues that the product development team should include product specifications, composition of the project team, a PERT/CPM chart to find out the critical path with key milestones, target dates

and implementation schedules. The marketing plan should not only specify the planned short term and long term roll-ours but also have identified risk factors, and suggestions for minimizing risk. Finally, the financial analyses should be expanded to include more detailed income statement and cash-flow information than was available at the proposal stage.

2.1.1. Supply chain of Pharmaceutical products

The concept of supply chain management has evolved from a narrow perspective, related only to material flows, to a broader view, encompassing material, information, financial and technical flows, both within each organization and between organizations (Arshider et al., 2008). Material flow and information are intrinsically connected in order to create service flows which are delivered to fulfill market needs (Mills et al., 2004). Thus, speed and accuracy are among the major concerns on managing information.

The literature on supply chain management could mainly be classified into three different flows: materials, Information and financial assets (Sahin and Robinson, 2002). As per the studies, delivering goods at the right place at the right time and related services constitute the material flow. It also revolves on issues of logistics, purchasing, stock replenishment, recycling and remanufacturing. Research suggests that order information and its propagation along the chain could be classified as Information flow (Lee et al., 1997), and initiatives like quick response and e-commerce. However, the management of financial flow has received much less attention to date. Although it is present in studies on supply chain coordination with contracts (Cachon, 2004)

Professor Davi Nakano and Marcelo Caldeira Pedroso (2009) did an in-depth case study on Pharmaceutical companies wherein technical flow needs to be managed apart from order information, using specially designed path. In Pharma industry customers do not have discretion over their purchasing decisions as they are dependent on physicians' prescriptions. Therefore pharmaceutical companies need to keep physicians well informed about drug development, in order to create demand. Thus these researchers argue that there have to be two paths in their outbound supply chain: the main path, where goods and order information flow to and from the market, and a secondary path, where technical information flows to create demand.

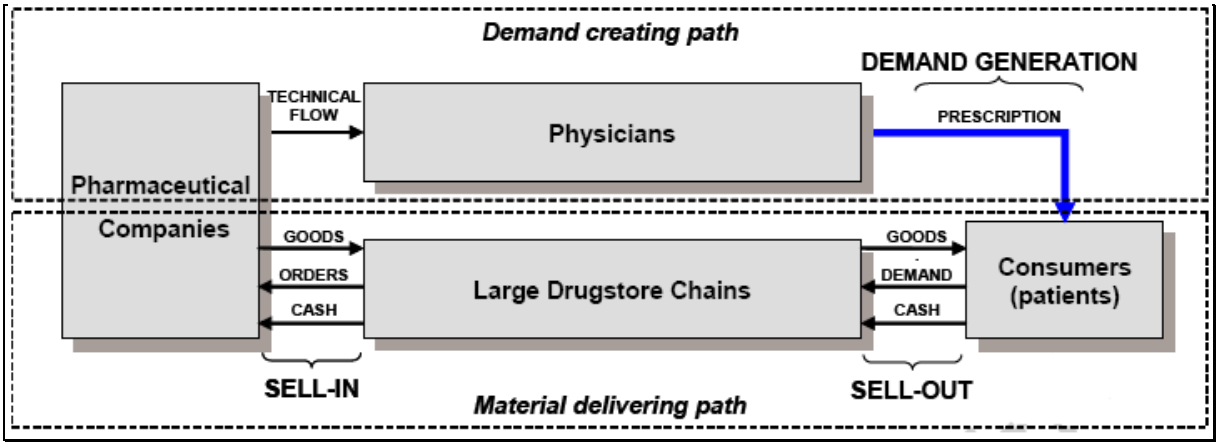

Figure 2: Demand generation in Pharmaceutical industry. Source: (Nakano. D, 2009)

The figure depicts two different paths:

- A material path, where products, order information and financial assets are conveyed, and
- A demand creating path, where technical information on drugs is delivered to physicians

The technical information flows upstream from Bio-Pharma companies to physicians however, the order information flow is from customers to drugstores and eventually pharma companies. Sell-in represents the flow of material in the drugstore and sell-out represents the product outflow to the patients. This demand is generated by the surgeon or the physician's prescription.

2.2. Life cycle of a Bio Pharma product

The potential of new technologies to increase the speed of bringing a product to market presents enormous opportunities. However, speed does not necessarily guarantee quality or therapeutic and commercial success. Development programs that are not founded on the principles of quality and rigor are destined for delay at best and failure at worst. Quality and not quantity must permeate every element of drug development.

Markets and technologies are changing rapidly, cost pressures are increasing, regulatory authorities are more demanding, and product life cycles and time-to-market are shrinking. Even with greater efficiency in lead identification and optimisation, improvements will also need to be made in clinical development and the overall speed to market. Gaining and sustaining a competitive advantage requires that a company understands the entire value delivery system, not just the portion of the value chain in which it participates. It can ensure technology providers access to the critical capabilities needed to seize opportunities from the major market developments. By providing strategies on when and how to access those technologies, a technology roadmap can help companies to position themselves better for the future (Rinne, 2004).

A research done by Amir Aslani (2008) indicates that the technology roadmap process starts with the endpoint or vision clearly in mind and then traces alternative technology paths to achieve it. This would need the organisations to have a roadmapping tool, the technology process and products that would require fulfilling the market demands. His research also explains the implementation of technology roadmaps that are both forward and backward looking, which are defined as follows:

Backward Roadmapping: Backward Roadmapping involves in finding out how to reach a given target set by the marketplace. Ultimately, the Bio-Pharma products are utilised within a consequent patient population and are thus market driven.

Forward Roadmapping: Developing of innovative Pharma products is largely technology-driven. Thus, forward roadmapping is the process of building upon existing technologies until new targets appear.

Figure 3 represents different stages of a product life cycle of a Pharmaceutical drug. Target discovery, drug discovery and pre-clinical trials would take 7 years, and the drug development process, which include clinical trials would take aproximately another 7 years. It would also need another 2 years to clear all the regulations and fill the marketing channels before it could be felt in the market.

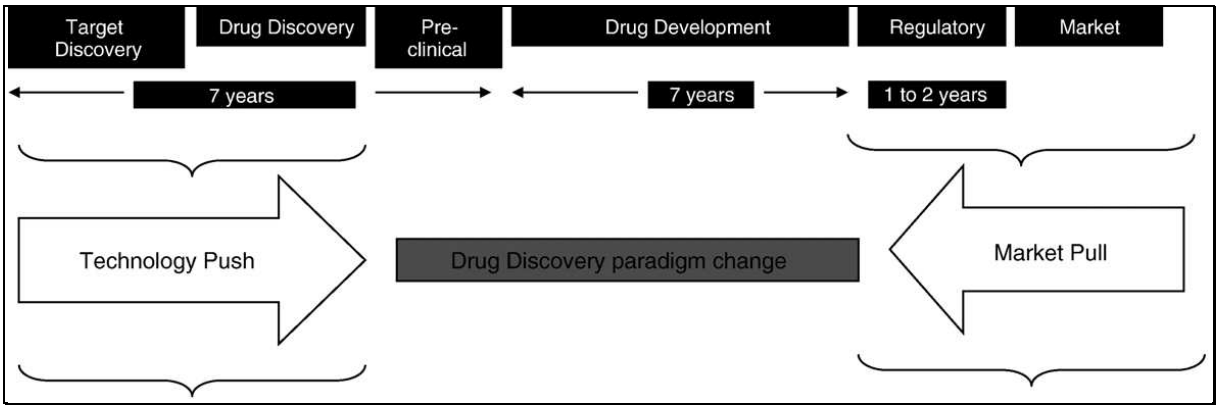

Figure 3: Driving forces of drug discovery paradigm change (Source: Amir-Aslani, 2008)

It could be challenging for any company to operate in this complex and uncertain environment. Therefore, through roadmapping, creative solutions to the technology issues and research needs could be identified. Technology roadmapping will also help a company optimize its strategic planning and business development framework (Phaal, 2004).

The Technology push as shown in the above (figure 3) is caused by one of the following fields: Informatics, Chemistry or Biology. Developments in biotechnology have allowed the drug discovery industry to move from serendipity based research towards rational, evidence-based approaches (Amir-Aslani, 2008). Technology pull would occur when the new bio-pharma product fulfills the fundamental requirements, such as:

- Satisfies unmet medical needs
- Exhibits superiority over existing treatments
- Safe with low adverse drug reactions

The research by Amir-Aslani (2008) also emphasizes on the fact that linking technology capabilities to future market needs in a resource constrained environment and high investor expectations would be the driving forces in drug discovery.

2.3. Tissue Engineering

Tissue engineering is an interdisciplinary field which applies the principles and methods of engineering and the life sciences towards the fundamental relationships in normal and pathological tissue and the development of biological substitutes to restore, maintain, or improve function (Skalak R, 1988).

Tissues that are engineered using the patient's own cells have the potential to overcome current problems of replacing lost tissue function and offer new therapeutic options for

diseases where currently no options are available. Tissue engineering technology can play a vital role in the future management of pediatric patients. The primary intention of all approaches in tissue engineering is the functional or structural restoration of tissue through the delivery of living elements which become integrated into the patient. Rapidly emerging field of tissue engineering presently uses a combination of cell based and matrix based to achieve new tissue formation (Saxena, 2005).

Cell and cell based techniques:

In cell based techniques, isolated and disseminated cells are injected into the blood stream or a specific organ of recipient. The cells transplanted using such injection methods will utilize the blood supply for nutrients and the ground substance provided by the host tissue as a matrix bed for attachment, reorganization and desired growth (Matas AJ, 1996).

Cell encapsulation techniques:

In this concept for cell transplantation, the cells are cultured and encapsulated in a semi permeable membrane that isolates the cells from the body. However, at the same time the semi permeable membrane, which allows the diffusion of nutrients and wastes, prevents macromolecules such as antibodies and immune cells from accessing the transplant (Rozga, 1994).

2.3.1. Tissue engineering using open systems of cell transplantation

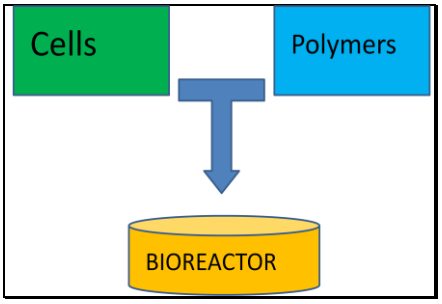

Figure 4: Schematic representation of the process of tissue engineering

The primary goal of the open system of cell transplantation is to engineer new tissues by having the transplanted cells in direct contact with the host with the intention of providing a permanent natural solution to the replacement of lost tissue. Cells for transplantation using this technique are attached to matrices consisting of natural materials or synthetic polymers and then implanted to the host.

This cell polymer construct then incorporates itself into the recipients own tissue. Therefore the approach to tissue engineering is to attach isolated cells to porous polymeric templates has been developed (figure 4).

<u>Biocompatible polymer matrices:</u>

An in-depth research done by Amulya K. Saxena in the Pediatric Surgical University Medical Center, Munster, Germany revealed few key characteristics that have to be prominent in an efficient biocompatible polymer matrix. His research findings revealed the following:

Polymer matrices used in tissue-engineered devices need to be biocompatible and have been designed to meet the nutritional and biological needs of the cell populations involved in the formation of new tissue. The next important feature is that the material should be re-

absorbable so that they leave a completely natural tissue replacement. Furthermore, polymer matrices should be reproducibly processable into desired structures and shapes and be able to retain their shapes after implantation in the host.

Finally, the surface should interact with the transplanted cells to allow retention of differentiated cell function. Materials on the other hand that do not possess the above properties or are non-reabsorbable carry a permanent risk of infection (Christiana AG, 1997). The most commonly used materials as substrates or encapsulating materials in the field of tissue engineering are either synthetic polymers such as lactic-glycolic acid or polyacrylonitrile polyvinyle chloride, or natural materials such as collagen, hydroxyapatite, or alginates (Saxena, 2005).

2.3.2. IN-VITRO Culture systems

In vitro (in the lab) culture systems that are mainly used for tissue engineering are Static Cell Cultures and Bio Reactors. During the field visit to IIT, Kanpur, it was found that Bio-Reactors were used for tissue engineered products.

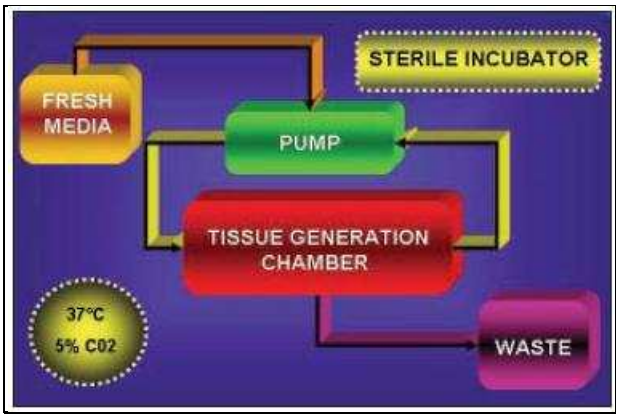

Figure 5: Dynamic cell culture or bioreactor concept for tissue generation using 3-D polymers
Source: http://www.jiaps.com

Bioreactors: Bioreactors are dynamic cell culture systems that allow more control to generate larger volumes of cells when compared to conventional static-culture techniques. (Figure 5) The flow of tissue culture medium and their mixing within bioreactors can be controlled to enhance mass transfer of nutrients, gases, and metabolites in order to regulate the size and structure of the tissue being generated.

Seeding of cells on 3-D biodegradable polymers in cell culture or flow bioreactor gave the opportunity to study tissue development, tissue regeneration, and tissue repair in vitro. Investigators have attempted to study the properties of almost all mammalian cell types under in vitro conditions. Knowledge obtained from different disciplines has evolved from primary animal research to clinical trials.

Since the focus of this report is mainly on skin regenerative templates for wounds and burn care, the present status of skin structural and fictional tissue has been described below:

Burn and burn related injuries are known to be associated with severe morbidity and mortality. In preclinical models, a cellular dermis has been populated with keratinocytes and fibroblasts and has been tested as skin substitute (Medalie DA, 1996). Biosynthetic analogs of skin, on the other hand have combined cultured skin cells with polylactic polyglycolic fabric, collagen sheets, and collagen-glycosaminoglycan sponges to provide skin re-placements. This approach involves the in vitro culture of keratinocytes obtained from small

skin biopsies of burn patients. The rapid expansion of the keratenocyte population is achieved by cultivating keratinocytes on a feeder layer of irradiated fibroblasts (NIH 3T3) in association with certain media components. Although this method could be used to cover extremely large wound; a disadvantage, however, is that 3-4 weeks are required for cell expansion (Saxena, 2005).

Another approach to fabricate skin, utilizes human neonatal dermal fibroblasts grown on degradable polyglycolic acid polymers. In this method selective cultures of dermal fibroblasts are inoculated into the porous reticulations of the substrate. In case of severe burn injuries involving all the skin layers, the graft is placed directly on the wound bed and a skin graft (cultured epidermal autograft) is placed above. This graft then vascularizes to form organised dermis like tissue. Furthermore, the addition of a dermal matrix to epithelial tissue engineered replacements adds the theoretical advantage of a thicker, more durable graft (Tinois E, 1991).

2.4. Research work on burns

There have been several studies done on the restoration of skin after a burn (2^{nd}/3^{rd} degree) or a wound. Most of the studies were done on products based on collagen or synthetic material. The area of gelatin being used as an alternative for collagen and indepth research into complete healing of the skin is still evolving. However, on analysing the research done on restoration of burnt skin there were was one crucial point which was evident in most of the work done:

While partial-thickness burns (1^{st} and 2^{nd} degree) have the ability to heal on their own while restoring relatively normal skin architecture, full-thickness burns (3^{rd} degree or deep wounds) do not. Full-thickness burn injuries that destroy both the epidermis and dermis produce irretrievable skin loss, since completely destroyed dermis does not regenerate. Although, a full-thickness burn wound may heal with a contracting scar tissue base and an overgrowth of thin epidermis, it lacks many of the normal structures and basic functions of skin. Temperature regulation, sensory perception, excretory function (through sweating), and metabolic activities such as the formation of Vitamin D, to mention but a few, are either severely compromised or completely lost (Chuong. et al, 2002). Thick and hypertrophied scarring is often the hallmark of burn healing.

Most burn surgeons interviewed during this research have pointed out the fact that skin grafting is most widely used to get a best outcome for the treating full thickness burns. Unfortunately, there is obviously only a limited amount that can be donated willingly from other parts of the body for transplantation. This therefore led researchers to explore either temporary skin substitutes or permanent skin substitutes (Jones, 2002).

Skin substitutes as a group, include a collection of varied topically applied agents that offer not just simple protective covering but also healing a burn. Such substitutes include products that have inherent healing properties of their own or have added biologically active substances, presumably able to advance wound healing (Hansbrough JF, 1998). They could either be sourced from intact human skin (called Allografts), animal skin (called Xenograft) or a combination of biological and manmade materials.

The most commonly used Allograft substitutes is frozen cadaver skin. Although Allografts have healing properties, it eventually succumbs to rejection by the patient's system when immune competence is restored. Various animals have been tried and tested for Xenografts. Among these, the best suited for this purpose is frozen pig's skin. However, it functions only as a temporary substitute or burn cover (Eisenbud D, 2004). Therefore the search for a true skin substitute is an ongoing process because of the inherent difficulties with Allograft and Xenograft.

A major development of skin substitutes came from Burke et al (1981) and the development of Integra® (Integra Life Sciences). According to Ravage, the development of Integra was the result of a collaborative effort by these two pioneers that dates back nearly 30 years. It was only in 1996 that Integra was approved by the United States. The product is marketed as a dermal regeneration template that allows the ingrowths of fibroblasts, vascular tissue, and cells in a more organised fashion. The bovine collagen in the dermis are replaced by the patient's collagen and cell ingrowths. The outer semipermeable silicone membrane functions as a protective barrier while revascularization and remodeling occur, much like normal epidermis. After maturation of the framework, this neodermis is covered by thin sheets of the patient's Autograft skin to complete the reconstruction (www.Integra-Is.com). This innovative discovery led to the outburst of many similar products. AlloDerm® (LifeCell Corp., Branchburg, NJ) is a dermal product that is made of specially treated cadaver skin. A proprietary process is followed to remove the epidermis and antigenic cells to leave a acellular, nonantigenic, dermal matrix (www.lifecell.com). Just as with Integra, AlloDerm must also be covered with skin Autografts to restore lost epidermis.

Compared to the Allografts and Xenografts, dermal replacement products offer many advantages. Firstly, the scar after healing is markedly reduced. Therefore the scar contracture procedures are reduced. Another at least semipermanent skin substitute is the patient's epidermal cells that are grown in the tissue cultures (discussed in above section). This technique allows the in-vitro cultivation of the patient's epidermal cells by modifications of the innovatory techniques described by Rheinwald and Green in 1975. However, this epicel cannot be considered as a total skin substitute unless used in combination with some form of dermal reconstruction, since it only restores epidermis.

Another product in the burn community often used as a temporary cover for burn is Biobrane™ (Smith & Nephew), It is perhaps equally used as often as skin donor site coverage. It is composed of two layers of silicone and a nylon mesh to which collagen is bonded (Smith & Nephew, 2009). Apligraf® and Dermagraft® (Advanced BioHealing) are two synthetic products that can be used as temporary skin substitutes, although their major utility appears to be in treating wounds other than burns. Apligraf is a man-made biological construct combining neonatal keratinocytes, fibroblasts, and collagen. Dermagraft uses either polygalactic or polyglycolic acid meshes combined with neonatal fibroblast to enhance wound healing (Advanced Bio Healing, 2009)

2.5. Summary

For the new product introduction the product differentiation would be crucial in estimating the target price of the product. Factors like price sensitivity of the market, the degree of competitive differentiation and possibility of competitive attack must be carefully evaluated. The supply chain of a bio-pharma product could be classified as flow of material, information and financial assets. The researchers suggest that there need to be two paths where there are not just goods and order information flow but also technical information flow is important to create demand.

Management gurus and research pundits also argue that it is not just the speed at which the products reach out to the customers but also the quality that permeates through every stage of the drug development that guarantees commercial success. In order to clear all the stages of a Bio-pharma's product life cycle, it is essential for a company to adopt strategies such as forward roadmapping or backward roadmapping. If the former strategy is applied then a technology push would be necessary by evidence based approach. However, if it is the later strategy, then technology pull would occur when the new product fulfills the fundamental requirements.

The techniques in the technology of tissue engineering that could be adopted are either cell and cell based or cell encapsulations. Research has proved that in biocompatible matrices, characteristics such as absorption capacity, extent of natural tissue replacement, ability to retain its shape after implantation in the host and the ability to retain differentiated cells are extremely important to prevent risk of infection. During the process of creation of an efficient matrix, an in vitro culture system like a bioreactor would play a pivotal role. Time and again, treating burns (2^{nd} and 3^{rd}) and deep wound has been a challenging task. Several researchers and organisations have invested time and money to regenerate skin so that it attains its original shape and texture. Unfortunately, the fact of the matter is that partial thickness burns have the ability to heal on their own during restoration, but, full thickness burns do not.

Chapter 3: Methodology

3.1 Methods for management research

The method adopted in this management report is a looping flow of information between academic knowledge (the literature) and empirical evidence to understand the situation and environment. The research could be classified based on the quantitative and qualitative data. Each of these functions within different assumptions. But, the approach adopted in this report is applying the quantitative data to qualitative research and vice versa.

3.1.1 Qualitative and Quantitative approaches

Based on book written by Merriam, S. B (1988) on 'Research in education: A qualitative approach' qualitative approach could be defined as follows:

Qualitative research is primarily process oriented, rather than outcomes or products. The interest is mainly in meaning how people make sense of their experiences, lives and their structures of the world. Therefore, it involves fieldwork to observe or record behaviour in its natural setting. It is more of a descriptive approach and involves understanding of the *actors'* perspectives.

Quantitative research as defined by Creswell, J. W (1994) is the primary instrument for data collection and analysis. Rather than through interviews, questionnaires, or machines, data is interpreted through human instrument. The purpose is to understand the trends and predict the future. The data is reduced to numerical indices and portrayed in an objective way.

Although some social science researchers (Lincoln & Guba, 1985) perceive qualitative and quantitative approaches as incompatible, others (Glesne, C., & Peshkin, A. 1992) believe that the skilled researcher can successfully combine approaches.

3.2 Chosen methodology for this research

Extensive secondary research was done to be abreast with the latest industry events and trends. Some of secondary information sources, where data was aggregated and analysed include:

- National/Governmental statistics
- International data (official international sources)
- National and International Bio-Pharma associations
- Broker and analyst reports
- Company Annual Reports
- Market Reports on Sector and Pharmaceutical industry
- Business information libraries and databases

Making revenue projections were based on the expected business strategies and financial analysis. Also, the Pharmaceutical industry standard was taken as benchmark to estimate the cost structure for the new product.

A qualitative and exploratory study, based on in-depth interviews, was designed to further understand how 2nd and 3rd burns are treated in India. Interviews were conducted in Bangalore, Chennai and Kanpur. Head of Department for Burns and duty surgeons of leading burns hospital- Victoria Nursing in Bangalore were interview on a Bi-weekly basis. A supplier of collagen based skin regenerating product in India was also selected for interviewing.

Interviews were conducted between June 2009 to August 2009, few were fully tape recorded, while others were only hand notes. Important documents were collected after the interviews. Interviews were later transcribed verbatim. Also, to assist analysis, from hand notes, documents and transcriptions, a description case was written, validated by informants and discussed. Although the number of informants was limited, data saturation was clearly reached, as no new concept emerged during interviews. Permission was granted to quote excerpts from the interviews.

3.3 Techniques to analysis

The secondary data from various market researchers, news articles and online reviews were collated to understand the global Pharmaceutical market. This was then compared to the Indian market and the Bio-Pharma industry in India. Based on this, the market segment for Skin and Wound management was carefully analysed. Various products that currently exist within the market and their characteristics were studied.

The information gathered by interviews about the existing product was crucial to understand the doctors' perspective and to understand the loopholes in the product life cycle of the existing skin regenerating products. Interviews with the suppliers helped to understand the challenges in the supply chain. Finally, the interview with the team in Kanpur that is developing the product helped to understand the product as a whole and where exactly it fits in the product life cycle. The conclusions and recommendations are drawn based on the as is condition with appropriate assumptions.

Chapter 4: Market Research and Analysis

To understand the Bio-Pharma market in India it is important to understand the current global Pharmaceutical market. Hence this section explores and analysis the international paharma market and narrows it down to the skin and wound regenerating products in the market. An attempt is made to focus on the Indian Biotechnology and Bio-Pharma market and gauge the market potential for the new skin regenerating product. The role of clinical trials in India and its effect on the new product is also analysed.

4.1. Market share

The global pharmaceuticals, biotechnology, and life sciences industry group is composed of the pharmaceuticals market, the biotechnology market, and the life sciences tools and services market.

The pharmaceuticals market includes only ethical drugs, ex-factory prices (the value at which manufacturers sell the drugs to distributors). The biotechnology market profile reviews companies primarily involved in the development, manufacturing or marketing of products based on advanced biotechnology research. The market value reflects revenues of companies within this market from product sales, licensing fees, royalties and research funding. The life sciences tools and services market is comprised of companies enabling the drug discovery, development and production continuum by providing analytical tools, instruments, consumables and supplies, clinical trial services and contract research services.

Year	$ billion	% Growth
2004	704.4	
2005	762.3	8.20%
2006	815.8	7.00%
2007	878.3	7.70%
2008	917.0	4.40%
CAGR, 2004-2008:		**6.8%**
Source: Datamonitor		DATAMONITOR

Table 1: Global Pharmaceuticals, biotechnology, and life sciences industry group value: $ billion, 2004-2008 Source: Datamonitor 2009

As per 2009 Datamonitor Report for the global pharmaceuticals, biotechnology, and life sciences industry the group generated total revenues of $917 billion in 2008, representing a compound annual growth rate (CAGR) of 6.8% for the period spanning 2004-2008. In comparison, the European and Americas industry groups reached respective values of $269.1 billion and $457.6 billion in 2008. The biotechnology segment generated revenues of $195.1 billion in 2008, equating to 21.27% of the group's aggregate revenues.

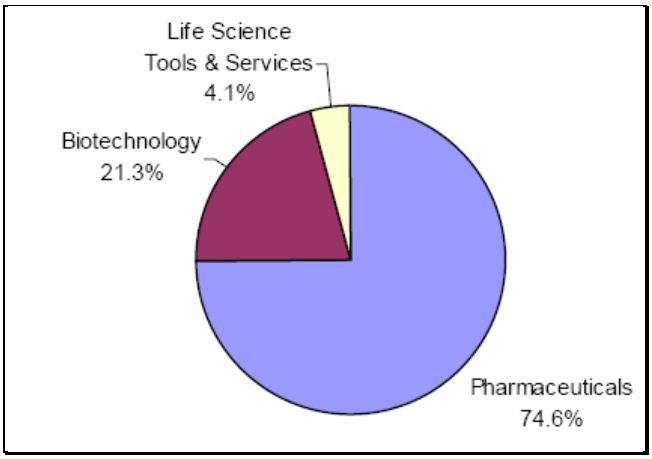

Figure 6: Global Industry group segmentation: % share, by value, Source: Datamonitor 2009

Pfizer is one of the world's largest research-based pharmaceutical company accounts for 5.3% of the global pharmaceuticals, biotechnology and life sciences industry group's value. The company is engaged in discovering, developing, manufacturing and marketing of prescription medicines for humans and animals. The company operates in more than 150 countries across the world (Pfizer Annual Report 2008). GlaxoSmithKline (GSK), along with its subsidiaries, constitutes one of the major global healthcare groups engaged in the discovery, development, manufacturing and marketing of pharmaceutical and consumer health-related products. After Pfizer, GSK accounts for a further 4.9% (Appendix) of the industry group's revenue. They have operations in approximately 117 countries, with products being sold in over 140 countries (GSK Annual Report 2008).

On further narrowing it down to Bio-Pharma sector, which is a part of Biotechnology, it accounts to 75.24% (Biospectrum-ABLE Survey 2005). Thus a large chunk of revenues in the Biotechnology industry accounts to the Bio Pharma sector.

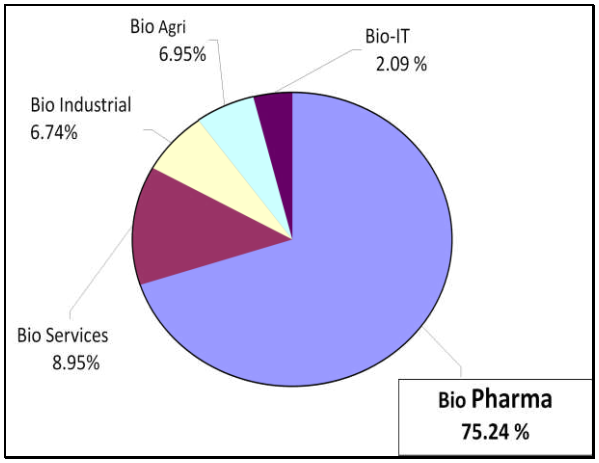

Figure 7: Bio-Pharma leads the way. Source:Biospectrum-ABLE Survey 2005

4.1.1. Why shift focus to India?

Indian Pharma:

Over the past few years the growth in the Indian pharmaceutical industry has been driven by rising disposable income, increased expenditure on healthcare, strong growth registered by Indian economy, changing diseases profile and regulatory forms. On overall basis, Indian companies outgrew the market at 11.9%; MNCs registered a growth of 5.5% (Cygnus Report 2009). The industry has seen tremendous progress in terms of infrastructure development, technology base and the wide range of products manufactured. Demand from the exports market has been growing rapidly owing to the capability of Indian players to produce cost-effective drugs with world-class manufacturing facilities. Bulk drugs of all major therapeutic groups, requiring complicated manufacturing processes, are now being produced in India. Pharma companies have developed Good Manufacturing Practices (GMP) compliant facilities for the production of different dosage forms. The Indian pharmaceutical industry is strengthening and mounting up the value chain. The industry, which was purely focused on reverse engineering, is now moving towards basic research driven market.

With slowing growth rates in developed markets, the fast growing emerging markets have emerged as new sustainable sources of revenue growth. Although, the current pharmaceutical market values in these countries are not impressive compared to more mature markets, most are experiencing tremendous growth rates compared to the modest 2-5% growth seen in the US and Europe. India has emerged as a key destination for global pharma companies because of its superior growth prospects, improving socio-economic profile and regulatory reforms. These initiatives have made India one of the key focus markets for MNC pharma companies (Emkay Research, 2009).

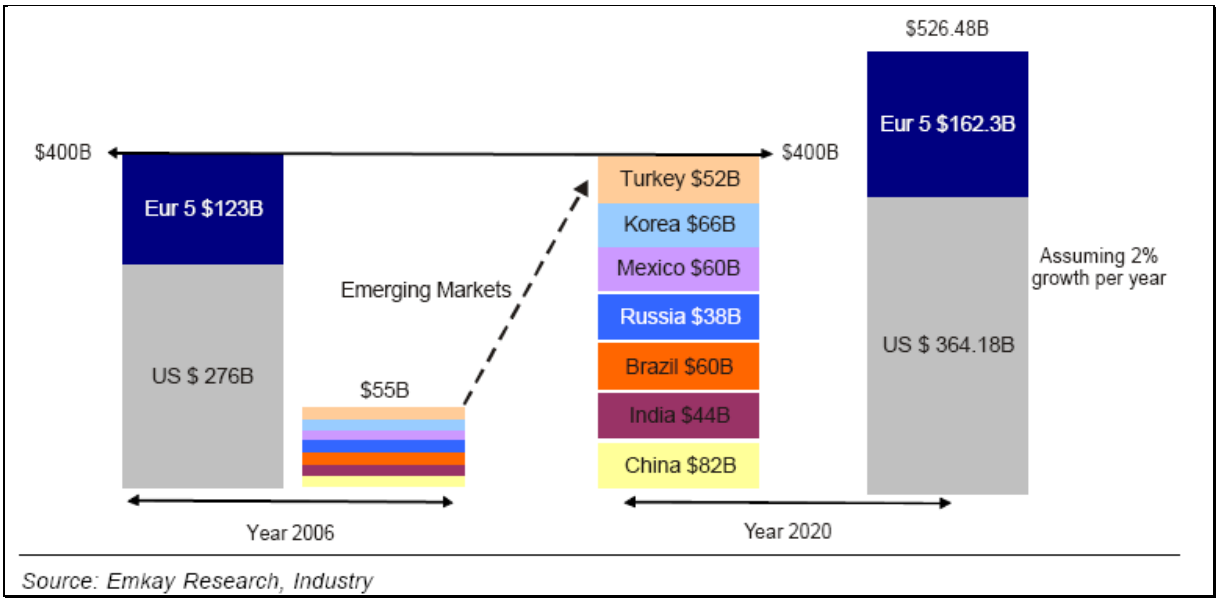

Figure 8: Growth in developing countries as against developed countries. Source: Emkay Research

In CY08, the growth in the developed markets came down to 3% compared to 12% growth in the emerging markets. Going forward, Emkay Research on Pharma industry is projecting a

2% CAGR in developed markets compared to a 15% CAGR in the emerging markets over CY06-20E. India occupies a significant position in the world Pharma market – especially in generics- 8% by volume (4th largest in the world) and 1.5% by value (13th largest). Export of generics accounts for 38% of the Pharma sector revenues (Virtus Global Partners, 2008).

Pharma sales of Top 10 MNCs in India

		(Rs bn)
1	Ranbaxy labs	74.06
2	GSK Pharma	18.33
3	Matrix Lab*	17.74
4	Aventis Pharma	10.7
5	Pfizer**	7.9
6	Abbott India **	7.07
7	Novartis India	6.17
8	Merck#	4.29
9	AstraZeneca Pharma	3.74
10	Wyeth*	3.61

*Note: *08 figures(Mar '09 figures not available ;** fiscal ending 'Nov.; #Subsidiary of German firm Merck KGaA; Source: Prowess, Cygnus Research*

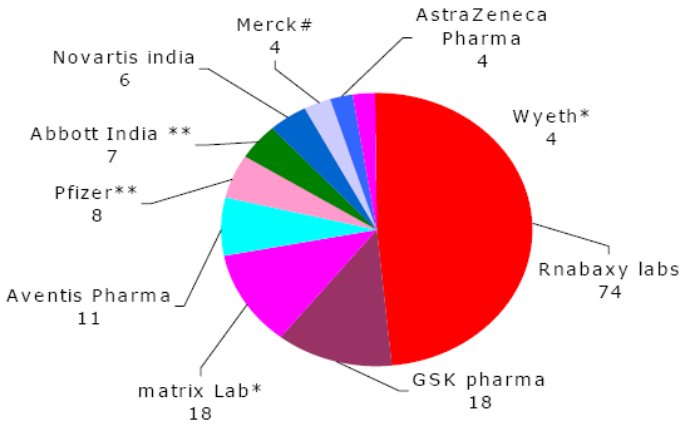

Figure 9: Pharma sales of Top 10 MNCs in India in 2008. Source: Prowess, Cygnus research

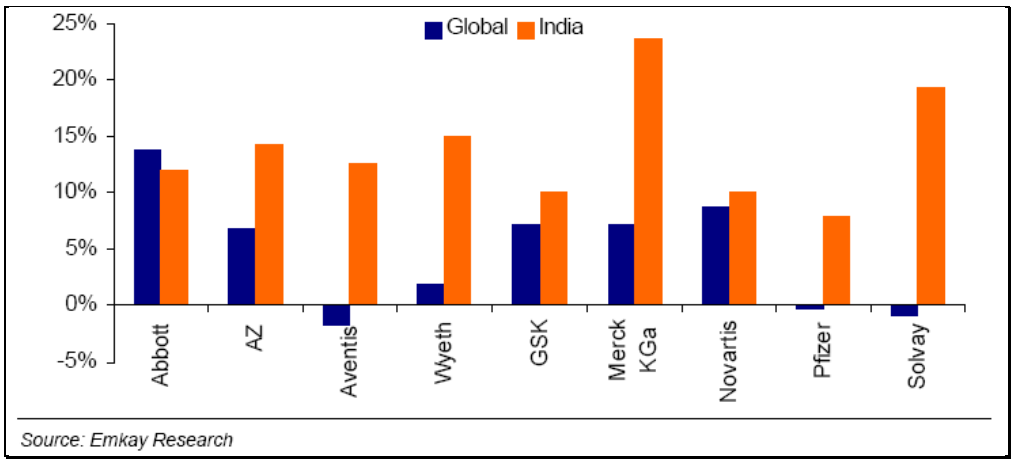

Figure 10: Indian subsidiaries have outperformed their parent companies. Source: Emkay Research

The above figure shows the pharma sales of top 10 MNCs in India it gives a clear indication on how the Indian subsidiaries of global pharma companies have outperformed their parent companies (albeit on a low base) in terms of sales and profit growth over the last 3 years. Most of the Indian subsidiaries have reported double digit growth in revenue, compared to the single digit growth of their parent companies.

As the MNCs are struggling for growth in the regulated markets, they are willing to allocate more resources to their Indian subsidiaries. Of late, most of the CEOs of parent companies have been vocal about their focus on the Indian market. GSK's global chief executive, Andrew Witty has emphasized the group's increased focus on emerging markets, including India, for future growth. Similarly, Sanofi-Aventis' global chief executive, Chris Viebacher has indicated that the company is looking at consolidation opportunities in India. Pfizer and Merck & Co. have increased marketing efforts in developing countries in Asia, including

India. In order to scale up its operation in emerging markets, MNC companies are adopting multiple strategies such as
a) scaling up of non-patented branded business
b) launch of patented products
c) divestment of non-core businesses
d) scouting for company/ brand acquisition and
e) charting country specific strategies.

4.2. Bio-Technology and Bio-Pharma Markets

The biotechnology market consists of the development, manufacturing and marketing of products based on advanced biotechnology research. The market value reflects revenues of companies within this industry from product sales, licensing fees, royalties and research funding.

The Global Wound Management market grew to reach a value of $584 million in 2001 (Datamonitor Report, 2001). This growth forecast by Datamonitor is at a CAGR of 17.8% between 2001 and 2011. It is evident that the potential for this market is very high due to the frequency of dressing changes and the slowness of the healing process. There are over 4 million chronic wounds every year in the global market, which provides a substantial opportunity for advanced wound care products. These dressings are only beginning to come into favour in many countries though, and many practitioners remain uneducated about the benefits of practicing moist wound care. The wound management industry thrives on volume. In fact, their research also states that many countries have such low profit margins that only wound care giants that bundle their products, or tiny local manufacturers can afford to sell their products in these countries.

: Global Wound Management Market Segmentation: % by Value, 2001

Sector	% Share
Alginates	11.8%
Amorphous Hydrogels	3.7%
Films	22.7%
Foams	21.1%
Hydrocolloids	36.1%
Hydrogel Sheets	4.7%

Table 2: Global Wound Management Market share, 2001. Source: Datamonitor Report, 2001

As per a 2001 report by Datamonitor on global wound management, Hydrocolloid are the most important type of wound management product in the Global Wound Management market, representing 36.1% of the market in value terms. Films and Foams each boast over 20% of the Market. Amorphous Hydrogels and Hydrogel Sheets both contribute to the Global Wound Management market and have just over an 8% share between them.

4.2.1. Bio-Technology in China

China has emerged as one of the key markets for global pharma companies. 10 countries contribute almost 85% of the total emerging markets sales. China is on the top among the emerging markets, contributing 25% of total emerging market sales and growing at the rate of 27%. India's contribution among the emerging market sales is 8% and is growing at 11% (Emkay Research, 2009).

Top 5 emerging markets- big and growing fast

	Rank	Market Sales	Share of EM Region	Market Growth
China	1	£10.7bn	25%	27%
Mexico	2	£4.9bn	11%	4%
Turkey	3	£4.9bn	11%	10%
Brazil	4	£4.8bn	11%	13%
India	5	£3.7bn	8%	11%

Source: Emkay Research, GSK Plc presentation

Table 3: Top 5 emerging markets in the Pharmaceutical sector, Source: GSK plc presentation 2009

As per the 2009 research conducted by Datamonitor on the Chinese biotechnology market, it was found that the market generated a total revenues of $6.3 billion in 2008, representing a compound annual growth rate (CAGR) of 18.1% for the period spanning 2004-2008. Also, the medical/healthcare segment proved the most lucrative for the Chinese biotechnology market in 2008, generating total revenues of $5.8 billion, equivalent to 91.5% of the market's overall value. In comparison, the food and agriculture segment generated revenues of $421.6 million in 2008, equating to 6.7% of the market's aggregate revenues (Datamonitor Report – Biotechnology in China, 2009).

One among the top players in the field, China National Biotech Group (CNBG) is a research-driven biotech company that discovers, develops, manufactures and markets a broad range of human health products, including vaccines, blood derivatives, biopharmaceuticals, diagnostic reagents and others. The company is also a major player in China for the import and export of scientific and medical equipment and materials (www.cnbgint.com).

4.2.2. Bio-Technology in UK

The UK biotechnology market has posted healthy growth rates over the past few years however 2008 saw the market enter a brief decline. Despite this the market researchers are expecting a quick return to low level growth for the coming years. The UK biotechnology market generated total revenues of $7 billion in 2008, representing a compound annual growth rate (CAGR) of 5% for the period spanning 2004-2008. In comparison, the French and German markets grew with CAGRs of 8.2% and 7%, respectively, over the same period, to reach respective values of $4.3 billion and $5.3 billion in 2008 (Datamonitor Report, 2009).

Year	$ billion	£ billion	% Growth
2004	5.8	3.1	
2005	6.2	3.4	7.30%
2006	6.7	3.6	7.50%
2007	7.2	3.9	7.80%
2008	7.0	3.8	-2.20%
CAGR, 2004-2008:			**5.0%**

Source: Datamonitor DATAMONITOR

Table 4: United Kingdom Biotechnology Market Value: £/$ billion, 2004-2008

There are two glaring market segments within UK which attract the Bio-Pharma companies. Firstly, the medical and healthcare sector has proved to be most lucrative for the United Kingdom biotechnology market in 2008, generating 69.2% of the market's overall revenues (Datamonitor Report UK Biotechnology Market, 2009).

Category	% Share
Medical/Healthcare	69.20%
Service provider	17.30%
Food & Agriculture	11.40%
Environment & Industrial processing	1.20%
Technology service	1.00%
Total	**100.0%**

Source: Datamonitor

Table 5: UK Biotechnology Medical/health care Market Segmentation: %Share, by Value, 2008

Secondly, on comparing UK with other European countries it accounts for 15.2% of the European biotechnology market's revenue. Although, it is second to Spain (16.6%), it still accounts to major portion of the continent's Biotechnology revenue. While life saving drugs in UK might be expected to display very low price sensitivity, it is rare for purchasing decisions to be made by patients: insurance companies or state run health services will aim to keep their spending down, and may have enough scale (or legislative power) to exert pressure on prices. Overall, buyer power in the biotechnology market appears to be moderate.

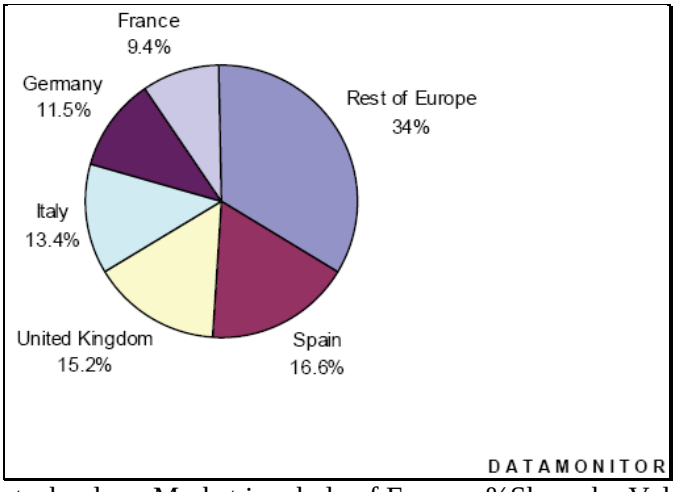

Figure 11: UK Biotechnology Market in whole of Europe: %Share, by Value, 2008. Source: Datamonitor

If we have to focus on the Bio-Pharma industry and Wound management in particular, the market segment has been very encouraging for the new skin regenerative graft. The market in the UK is rapidly evolving, due to the combination of high product availability and the use of the National Health System to promote these products. The pie chart (figure 12) below gives a clear indication of the wound management techniques that account to maximum share in terms of demand (revenue) and popularity. Hydrocolloid[1] based products account for the largest sector of the United Kingdom Wound Management market, representing 33.8% of the market in value terms. Foams[2] account for 27.4%, while Hydrogel Sheets[3] have 10.6% of the market share. Amorphous Hydrogels[4] is the smallest sector of the United Kingdom Wound Management market, representing 2.9% of the market in value terms.

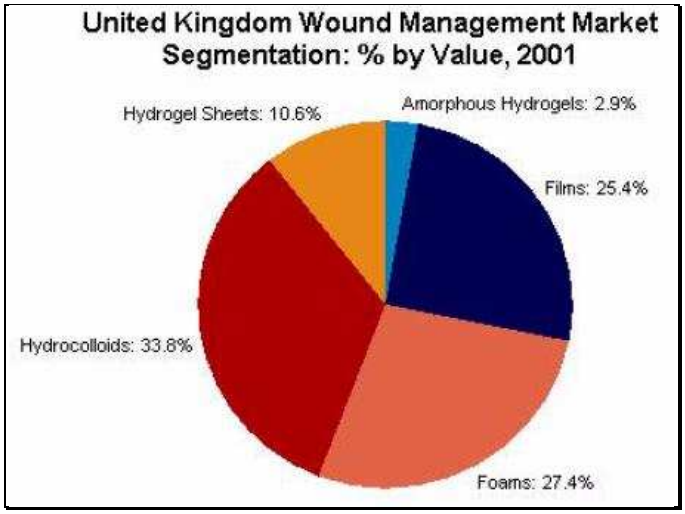

Figure 12: UK Wound Management Market, Source: Datamonitor, 2001

4.2.3. Bio-Technology in Asia-Pacific

The Asia-Pacific biotechnology market generated total revenues of $45.1 billion in 2008, representing a compound annual growth rate (CAGR) of 10.1% for the period spanning 2004-2008. In comparison, the Americas and European markets grew with CAGRs of 13.8% and 8.5%, respectively, over the same period, to reach respective values of $125.1 billion and $46.1 billion in 2008 (Datamonitor Report, 2009). Just as the case in China and UK, the medical/healthcare segment proved the most lucrative for the Asia-Pacific biotechnology market in 2008, generating total revenues of $29.1 billion, equivalent to 64.7% of the market's overall value. In comparison, the food and agriculture segment generated revenues of $12.5 billion in 2008, equating to 27.7% of the market's aggregate revenues (Datamonitor Report Biotechnology in Asia-Pac, 2009).

[1] These dressings mix with wound exudate to form a soft mass that allows for easy removal while protecting the wound from outside contamination from bacteria, fecal matter or urine.
[2] Foam sheets are hydrophilic in nature, so can absorb a large amount of fluid, and provide a soft and cushioning layer for added patient comfort. They are easy for clinicians to apply and to remove, with minimal trauma to the patient and to the wound bed.
[3] Hydrogels are useful for rehydrating sloughy or necrotic (dead) tissue and enhancing autolytic debridement. Patients like hydrogel sheets due to their cooling and soothing properties upon application.
[4] Amorphous Hydrogels are useful for rehydrating sloughy or necrotic tissue and enhancing autolytic debridement.

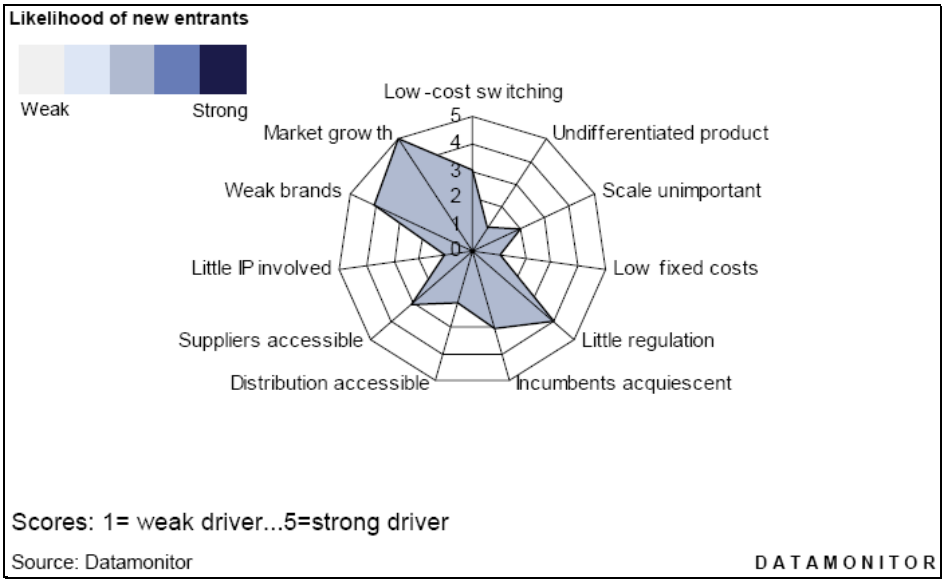

Figure 13: Factors Influencing the Likelihood of New Entrants in the Biotechnology Market in Asia-Pacific, 2008

The likelihood of new entrants moving into the biotechnology market appears to be moderate based on the above figure for the Asia-Pacific market. Biotechnology start-ups are typically spin-off companies based on innovative products or processes resulting from discoveries in academic research. There is therefore a high degree of proprietary knowledge and products within the market, which restricts the entrance of new players. A 2009 Datamonitor Report on the Asia-Pac Biotechnology companies typically suggests that they have long start-up periods with little profit, combined with high fixed costs, and therefore must secure a high degree of venture capital backing. This may be difficult to obtain, given the long time before any return on investment is seen, and the relatively high risk that a start-up will not succeed in bringing a new product to the marketplace. Despite this, the report also suggest that a high level of growth of the biotechnology industry within Asia-Pacific, combined with a relative lack of restrictive government regulation of biotechnology operations compared to western regions is attracting significant biotechnology investment within the region. This is especially true of countries such as India and Singapore, which have a highly significant biotech sector.

4.2.4. Bio Technology and Bio-Pharma in India

The Pharmaceutical industry in India is fragmented with over 3,000 small/medium sized generic Pharma manufacturers. International pharmaceutical majors like Pfizer, Johnson & Johnson, Glaxo SmithKline and Novartis have an established presence in India. The Biotech Industry is seeing the emergence of several domestic private players with world-class capabilities. Major opportunities in Biotechnology are in the areas of Bio-informatics, Biopharma, Bio-agriculture and Bio-services. Many international biotech companies like Chiron Corp, GSK and Sigma Aldrich Corp have expressed interest especially in Bio-manufacturing (Virtus Global Partners, 2008).

Department of Biotechnology (DBT) and the government of India have invested more than Rs.25 million to date in biotechnology. The biotech industry is one of the fastest growing sectors in India, with investment growing six-fold from 2000-2003 according to government sources. In 2005/06, the Indian biotechnology industry registered turnover of more than US$1.5 billion according to the DBT, with growth of 40%. By 2010, annual turnover is projected to reach US$10 billion (DBT Annual Report 2008-09). The figure below shows the Pharma sales of top 10 domestic companies.

Pharma sales of top 10 domestic Pharma companies

		(Rsbn)
1	Dr.Reddy's	69.44
2	Cipla	43.07
2	Sun Pharma	53.38
4	Lupin	38.23
5	Wockhardt*	35.92
6	Piramal Healthcare	33.13
7	Aurobindo Pharma	30.56
8	Cadila Healthcare	29.47
9	Glenmark Pharma**	20.13
10	Torrent Pharma**	13.78

**Dec ending fiscal 2008 figures(2009's are not available); **2008 figures(2009's are not available); Source Prowess, Cygnus Research*

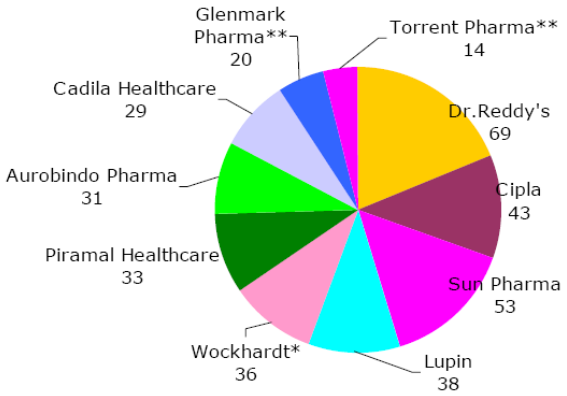

Figure 14: Pharma sales of top 10 domestic companies. Source: Cygnus Research, 2009

4.3. Regulatory Environment

Since Bio-Pharma falls under Biotechnology sector, a brief overview of the regulatory framework and government policies on Biotech Sector as a whole is analysed in this section. The regulatory framework in Biotechnology is undergoing a huge revamp and hence Biopharma sector is also expected to be affected by it. Though there are no specifically separate regulations and policies for the Biopharma sector, there are few aspects of the upcoming Biotech policy which will affect the Biopharma sector.

4.3.1. Government of India Policy on Biotechnology

The Department of Biotechnology (DBT) is the nodal agency for policy, promotion of R&D, international co-operation and manufacturing activities, which was set up in 1985. During the middle of 1980's, DBT focused on generating trained manpower and infrastructure development.

The other government agencies involved in biotechnology R&D are

- Indian Council of Medical Research (ICMR),
- Indian Council of Agriculture Research (ICAR),
- Council of Scientific and Industrial Research (CSIR) and
- Department of Science and Technology (DST).

In addition to the Central Government initiatives, several states have formulated their state specific biotech policies to boost the biotechnology sector in their respective states. Out of the six regulatory bodies in India (Appendix G), the most relevant one for the new skin

regenerating graft would be Drug Controller General of India, Ministry of Health - which is the official regulatory body governing manufacture and commercial release of pharmaceutical products, including recombinant products

India's Intellectual Property regime is a dimension in facilitating collaborative activity, whether for drug discovery, clinical trials or for market-related trials.

4.3.2. Funding Agencies in Biotech Research

Institutional Framework

At present, there are seven major agencies in India responsible for financing and supporting research in the realm of biotechnology apart from other sciences. They are:

DST (Department of Science and Technology), DBT (Department of Biotechnology) and DSIR (Department of Scientific and Industrial Research) are part of the Ministry of Science and Technology; while ICMR (Indian Council of Medical Research) is with the Ministry of Health, ICAR (Indian Council of Agriculture Research) with the Ministry of Agriculture and UGC with the Ministry of Human Resource Development

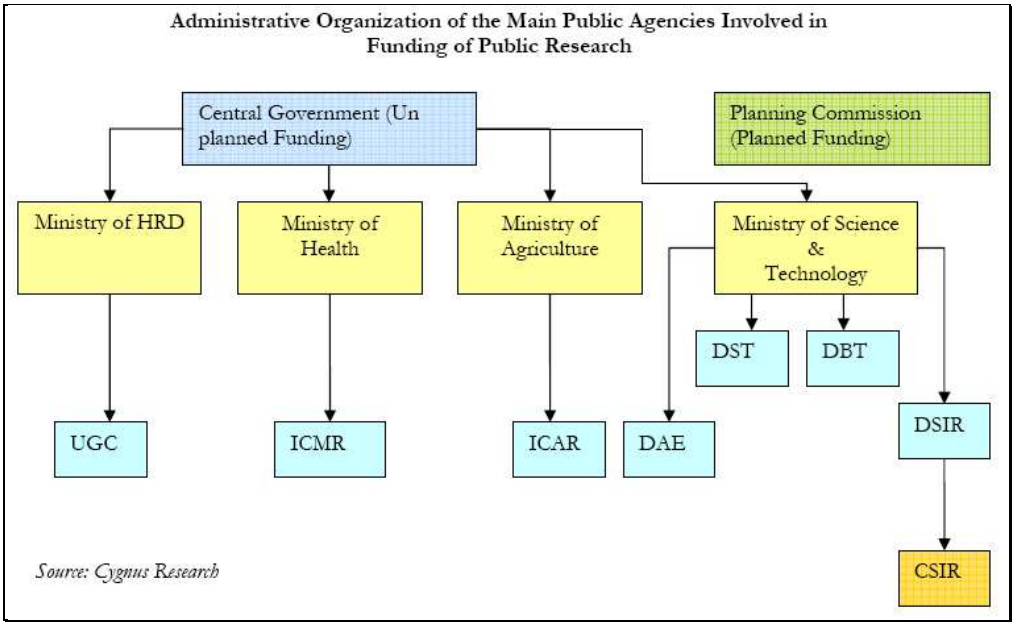

Figure 15: Institutional Framework and Public Sector Research Support.
Source: Cygnus Research

Foreign Direct Investments

Foreign Direct Investment (FDI) is seen as a means to support domestic investment for achieving higher level of economic development through technology upgradation, access to global managerial skills and practices, optimum utilization of human and natural resources, making Indian industry internationally competitive, opening up of export markets and providing linkages and access to international quality goods and services.

Incentives for investment in biotechnology industry and R&D

- 100% foreign equity investment is possible in almost all sectors.
- 100% foreign equity investment is automatic in drugs and pharmaceuticals sector, and over 74% is on case by case basis.
- Fast Tract Clearance route for FDI.
- Depreciation allowance on plant and machinery set-up based on indigenous technology.
- Customs duty exemption on goods imported for use in Government funded R&D projects.
- 125% weighed tax deduction on R&D expenditure.
- Three-year excise duty waiver on patented products.
- 100% rebate on own R&D expenditure.
- 125% rebate if research is contracted in public funded R&D institutions.
- Joint R&D projects are provided with special fiscal benefits.
- Customs and excise duty exemptions to recognise Scientific and Industrial Research Organisations.

Source: dbt.nic.in

Venture Capital funds

With the increased role of established private sector as well as start-up companies investing in biotechnology, several financial institutions/agencies, both in public and private sectors, have launched venture capital (VC) funding mechanism. The Ministry of Science and Technology created these opportunities through the establishment of Technology Development Board (TDB) in September 1996 for providing financial assistance to industrial concerns and other agencies attempting development and commercialization of indigenous technology or adopting imported technology for wider domestic application (http://www.tdb.gov.in/).

Banks continue to remain the major financing source for biotechnology in India with VC accounting for less than 20% of the funding (Cygnus Business Consulting & Research 2008). In 2003, the first national VC fund for biotechnology in India - The Biotechnology Venture Fund - was initiated. It was started with APIDCVCL, a joint venture between Dynam Ventureast Group and Andhra Pradesh Industrial Development Corporation (APIDC, Hyderabad, India). In 2004, it provided about INR 800 million (USD17.7m) in funding the biotech firms (www.apidc.org). Given the reluctance of existing venture capital funds to invest in early stage developments, APIDCVCL is targeting early stage tech businesses.

4.3.3. National Biotech Development Strategy

Government of India in 2005 came up with the National Biotech Policy Draft which talks about the future road map for biotechnology for a period of 10 years. Some of the Key policy recommendations & interventions in the area of biopharma mentioned in the national biotech policy draft are discussed below (National Biotech Development Strategy, 2007)

Regenerative Medicine:

The first wave of real healthy life extension therapies seems likely to result from research stem cells and regenerative medicine which helps natural healing processes to work faster, or uses special materials to re-grow missing or damaged tissues. Doctors use regenerative medicine to speed up healing, and to help heal injuries that cannot heal on their own. Regenerative therapies have been demonstrated (in trials or the laboratory) to heal broken bones, bad burns, blindness, deafness, heart damage, nerve damage, Parkinson's and other conditions. Regenerative medicine will result in an extended healthy lifespan; which will repair the damage caused by ageing, organ by organ.

Bioengineering:

Bioengineering covers a wide range of areas such as tissue engineering, biomaterials for therapeutics, biomedical devices and instrumentation, biomedical sensors etc. Research is focused on developing non-immunogenic materials to serve as scaffolds for regeneration of damaged tissue. Bone and cartilage can be grown today while there is potential for other tissues too.

The **current market** for medicinal devices such as implantables, **disposables wound care**, dental and orthopaedic materials etc is estimated at around **INR 70 billion** and another INR 50 billion for the medical instrumentation sector in the country, with a growth rate of 15% per year (Cygnus Business Consulting & Research 2008). Nearly 80% of this demand is met by imports.

4.4. Clinical Trials Market in India

Contract research involves outsourcing of various activities relating to R&D to Indian pharmaceutical companies by global companies. Contract research includes both drug discovery research and clinical research. According to a report given by McKinsey, clinical trials comprise 65% of the contract research market and new drug discovery makes up remaining 35%.

The new skin regenerative graft or any other bio pharma product has to undergo clinical trials before entering the market. The different phases are mentioned in the figure starting from Drug discovery and all the way to Post marketing testing. Clinical trial is the final step in drug development process after preliminary laboratory research and animal testing. Some of the questions considered during this research were- Is India the best place to conduct clinical trials for this new product? If yes, what are the advantages and disadvantages?

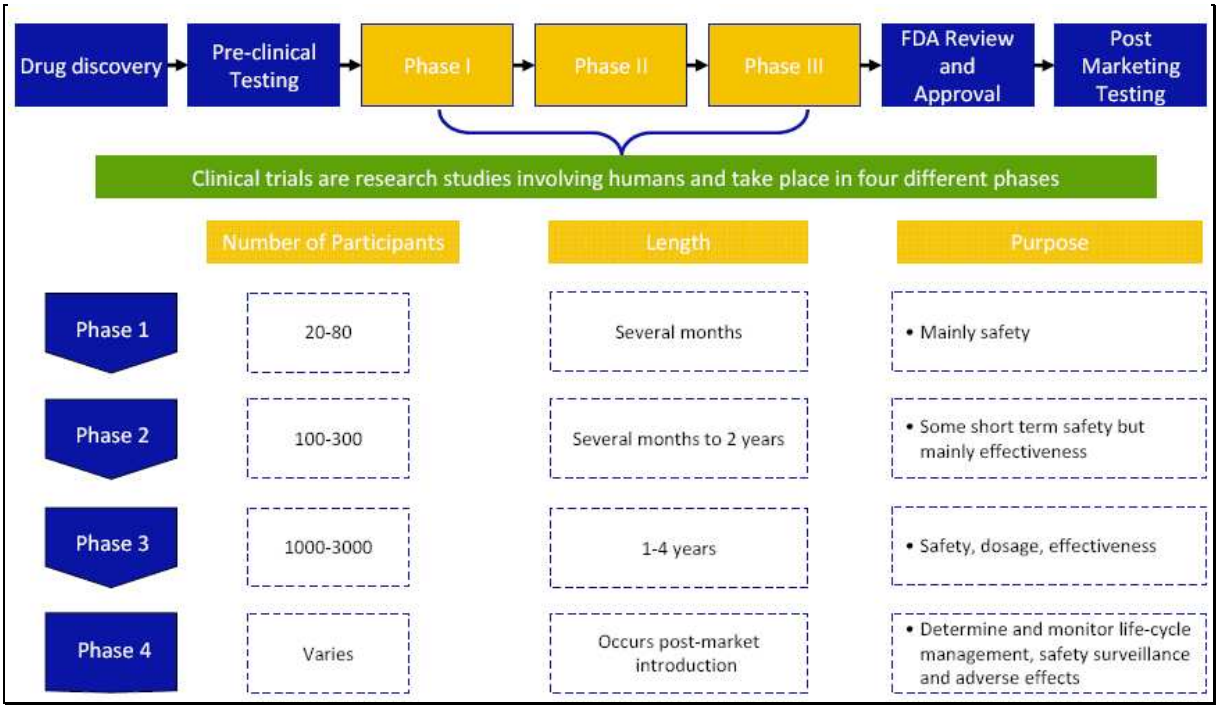

Figure 16: Phases in drug development process. Source: *"Clinical Trials Industry in India" February* 2008 *; Indipedia " Clinical Trials" ; Myeloma Canada " clinical trial FAQs"*

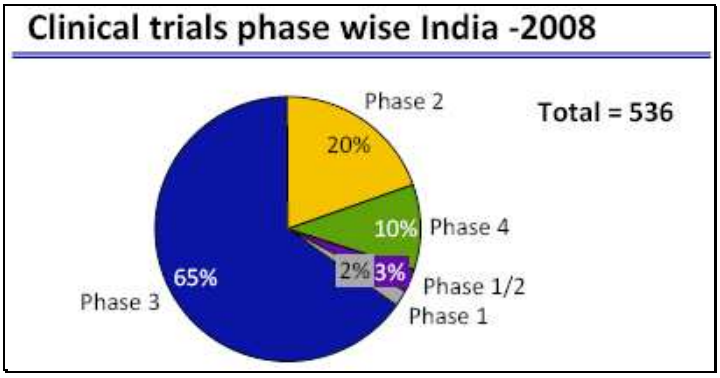

Figure 17: % distribution of clinical trial phases, Source: RNCOS

In 2008, there was an increase in clinical trials by 143% from 2007. Among the total number of clinical trials conducted in the year 2008, 65% of them were in phase 3. This indicated the time taken for FDA review and approvals would take the maximum amount of time. On the contrary, phase 1 has the least time delay with just 2% (fig 17).

If we have to weigh the pros and cons of conducting clinical trials in India then few key observations are as follows:

Cost Effectiveness:

India offers significant cost savings in clinical trials. Multinational pharmaceutical companies can achieve cost savings of around 30–50% when outsourcing clinical trial projects to India (Companies and Markets Research, 2009). In the US, it might take nearly three years to get around 100 patients to conduct trials on them, in India the same number could be gathered in about six months.

Phase	US Costs	Indian Costs
Phase I	USD 20 mn	<USD 10 mn
Phase II	USD 50 mn	<USD 30 mn
Phase III	USD 100 mn	<USD 60 mn

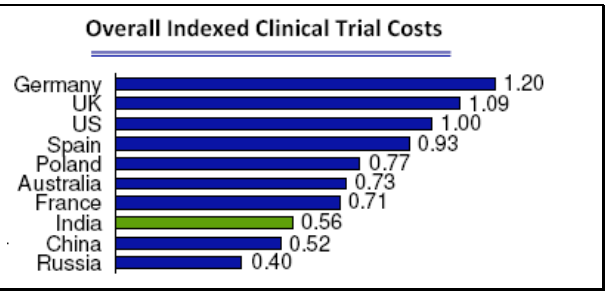

Figure 18: India – Cost competitiveness. Source: Companies and markets Research, 2009

Sound Healthcare Infrastructure:

Indian Healthcare Infrastructure - 2006	
Public Hospitals	4,049
Private Hospitals	11,334
Hospital Beds	875,000
Doctors	1,000,000
Medical Colleges	221
New Doctors every Year	18,000
Retails chemist Outlets	350,000
Dental Colleges	100
Pharma Colleges	150

Table 6: Sound Medical Infrastructure.
Source: (Indian Panacea, 2006)

India has established world-class expertise in complex medical practices such as cardiac care, cosmetic surgery, joint replacements, neurosurgery, ophthalmology and dentistry at par with the best hospitals in US and UK. They offer huge array of tailor-made options such as private room, translator and private chef. All medical investigations are conducted using the latest, technologically advanced and cutting edge diagnostic equipment. Indian pharmaceuticals meet the stringent requirements of FDA. Table 6 is a snapshot of India's healthcare infrastructure (Indian

Despite the above advantages from clinical trials in India, there are few glaring disadvantages that could hamper the growth in this sector.

Shortage of Research Professionals and lack of data exclusivity:

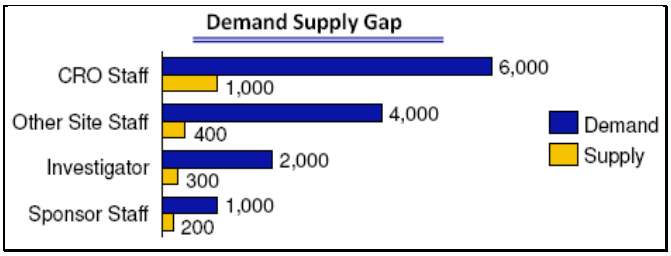

Figure 19: Mismatch in Demand and supply
. Source: AceIndia

India is facing a shortage of Good Clinical Practice (GCP) certified sites and investigators (figure 20). Over the next five years about 1,500-2,000 good clinical practices (GCP) trained investigators supported by 50,000 clinical research professionals would be required in India (Ace India, 2006).

The Indian law has no statutory protection for the data that is submitted to regulatory authorities for testing for approval of any manner of products. Although India is a signatory to the TRIPS[5] Agreement, no new provisions of law have been introduced to protect test data. The existing legal provisions are inadequate and compensation-focused. The requirements of data protection and exclusivity obligations are proactive in nature, i.e. focused on preventive

[5] Trade Related Aspects of Intellectual Property

mechanisms. There is no legislation corresponding to the "Hatch Waxman Act[6]" (Jaya Bhatnagar, 2009).

Delays in trial approval and challenges of unethical trials:

Delays in granting approvals are affecting pharmaceutical companies and CRO[7]s in India. Delays happens as the Drugs Controller's office depends on external experts and agencies such as Indian Council of Medical Research for advice and additional permissions required for import of trial samples and export of samples to foreign laboratories (Thaindia, 2008).

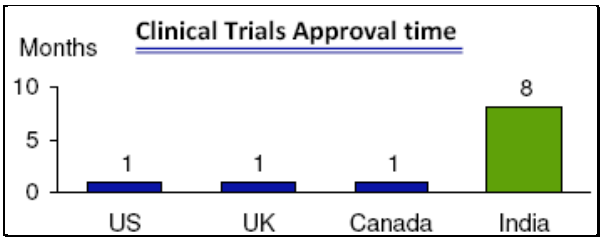

Figure 20: CT approval time in India
Source: thaindia

"India takes a minimum of eight months to accord clinical trials approvals whereas in Canada, the UK, and the US, clinical trials *approval are given in a month's time,"* The Associated Chambers of Commerce and Industry of India (ASSCHAM) senior vice-president Swati Piramal said

The clinical trial business is dependent upon a large pool of human subjects - or, a stable of human guinea pigs - in who the drugs are tested. But with increased awareness of the risks involved in testing drugs under development, the pool of human volunteers in industrialized countries has shrunk. The drug industry is looking for alternatives to carry forth the much need trials. Therefore they are increasingly moving to underdeveloped countries where they are enrolling uninformed, non-consenting people who have few choices in life. Unfortunately, India is a target drug testing population. A spate of unfortunate events over the past few years has brought to the fore the rampant practice of conducting unethical and even illegal clinical trials (Clinical Research 2008).

Supreme Court of India had hauled up two top biotech companies Shanta Biotech & Biocon for openly conducting illegal clinical trials of new drugs on unsuspecting patients after a litigation filed by Aadar Destitute and Old People's Home (an NGO). NGO alleged that the two companies had conducted improper clinical trials of Streptokinase - a new clot-busting drug used in heart attacks without requisite permissions, as a consequence eight people lost their lives (Asia Times, 2004).

[6] In 1984 the US became the first country to enact data exclusivity legislation. The Drug Price Competition and Patent Term Restoration Act, commonly known as the "Hatch-Waxman Act", actually relaxed the level of protection afforded to testing data in the US. Under the Hatch-Waxman Act, applications for approval of new drugs receive 5 years of data exclusivity. Applications for the approval of new indications for an existing drug receive 3 years of data exclusivity.

[7] Contract Research Organisation

4.5. Skin Regenerating Grafts for Burns and Wounds

4.5.1. Background

The outermost layer of the skin is called epidermis. The cells involved here are called keratenocytes. If the top layer is destroyed it can be easily regenerated. The layer below is a thicker layer called Dermis. The cells involved here are called fibroblasts. Majority of the products that are currently available in the market are aimed at healing damaged dermis layer of the skin.

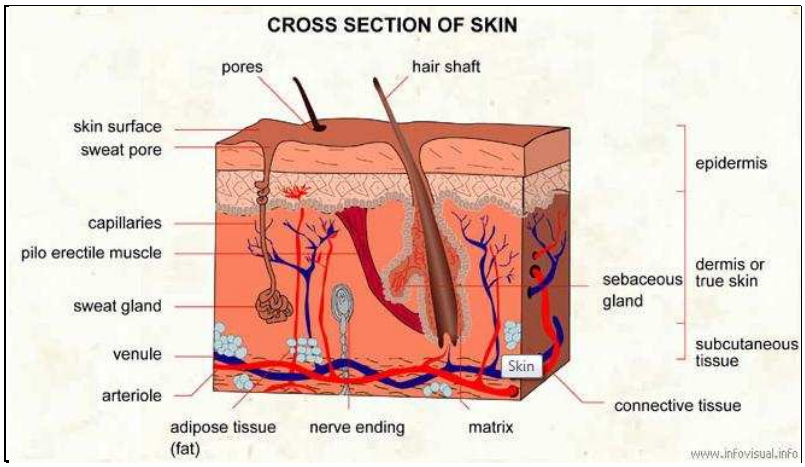

Figure 21: Cross Section of Human Skin. Source: infovisual.info

During the healing process the major challenge is to prevent infections from occurring. On successfully doing this "95% of the battle is won" says Dr Ashok Kumar. Dressings, including normal band aid, could be classified under this segment. The different types of burns characteristics could be defined as follows (www.burnsurvivor.com):

1st Degree burns: Involves top layer of skin and hair, redness, swelling. It may peel, generally heals in 3-5 days. There is no scaring and may cause itching while healing.

2nd Degree burns: Involves skin and hair, plus deeper skin layer (dermis), sweat glands, and hair follicles. It results in blistering, redness, area turns pale when pressure is applied, red color returns slowly.

3rd Degree burns: Involves all thickness of outer skin including fatty layer. Looks dry or leathery, may be charred. There is little or no pain (nerve endings have been damaged), Greater possibility of infection, since blood supply to area is damaged. This results in scarring post healing.

Skin regenerative template/grafts/tissue engineered scaffolds main purpose is to allow the cells to grow and the wound dressing prevents any infections form taking place during the healing process. For assisting this regeneration of cell in the affected area a scaffold is used. Generally they are 2mm to 4mm in thickness.

4.5.2. Products in the Market – An Overview

The field of skin substitutes has been bombarded with almost Messianic zeal in an effort to develop the next generation of newer and better skin replacements. These dressings are made with varied combinations of synthetic and/or biologic substances. Although all may have some utility and each has its champions, they appear to find more application in the larger and therefore more lucrative wound market. Few of the popular companies in the market who make products which are used for treating 2nd degree burns and wounds are mentioned in table below. This research is focused on burn products which are scaffold based.

Name	Description	Website
Invitrx INNOVATIVE TISSUE ENGINEERING	Innovative Tissue Engineering for wound closure, corneal transplants, and adult stem cell therapy in cosmetic surgery and other clinical indications	www.invitrx.com
EnColl	Helicoll is a Type-I collagen sheet used for treating 1st and 2nd degree burns and wound dressing	www.encoll.ocm
LifeCell A KCI Company	AlloDerm®: Regenerative Tissue Matrix: improving functional outcomes and cosmoses in grafting procedures	www.lifecell.com
INTEGRA	Integra™ Bilayer Matrix Wound Dressing for partial and full-thickness soft tissue trauma and chronic wounds	www.integra-ls.com
MEDIRA SPECIALIST SUPPLIER OF MEDICAL PRODUCTS	Neuskin-F™ is an effective epidermal substitute that supports epidermal cell attachment and migration	www.medira.co.uk

A comparative study was done to understand the characteristic features of these collagen based products and how they differ from one another. The results of the study and a broad overview are mentioned below:

Type	Characteristics	Drawbacks
Integra™	• Single layer of Glycosaminoglycan and a covering semi-permeable polysiloxane (silicone layer) • Exceptional Strength and flexibility • Room temperature storage and long shelf life • Provides excellent coverage over exposed bone, tendon, cartilage and joints. Of 166 instances of exposed internal structures that are ordinarily closed with flaps, Integra closed 90% of them (Jennifer Furman, 2004)	• Very Expensive • Not used globally • Extreme care must be considered during packaging and transportation (Total Recall 2009)
Neuskin-F™	• Collagen dressing derived from Piscean sources: Biocompatible as per EN ISO 10093 standards. Non-toxic, non-allergenic, non-immunogenic, non-	• Avoid in patients hypersensitive to fish products. Chances of

	pyrogenic (Gottlieb, 2004) • Transparent membrane enables wound visualization. Reduces wound pH, infection and fluid loss (Hampton S, 2008) • Epidermal substitute for scald burns, superficial partial thickness burns (IIA) and mixed burns **Storage:** Dry place at temp < 25ºC. It is sterilized by irradiation with 3yrs shelf life (Kilinc, 2001).	Irritation and Infection. The remedy for this is to either discontinue or control with systematic antibiotics respectively (Shukla VK 2007)
HeliColl™	• Type-I Collagen sheet with transparent membrane enables wound visualization • Does not require excessive washing to remove preservatives. Can be used with just 2 to 3 min of soaking in sterile water. • Reduces wound pain while accelerating tissue remodeling without causing irritation • Helicoll reduces the repeated dressings, hospital stay and has been shown to reduce the overall wound treatment cost by over 40% (Advanced-Biotech, 2009).	• Not advisable for patients hypersensitive to bovine products. • Non adherent secondary dressing is required to maintain moist wound environment. • Helicoll may form a caramel coloured gel, which can be rinsed away with gentle irrigation. • Can be used only for 1st and 2nd degree burns trauma with skin loss, chronic skin ulcers Skin donor sites

4.5.3. Existing Cutting edge technology in India for treating burns

"**Artificial Skin**" by National Institute of Immunology (NII), New Delhi:

NII have developed a novel "surfactant mediated fusion process" resulting in self-assembly of polylactide particles into membrane like structures at room temperature named as ARTSK-NII. These are made from FDA approved biodegradable polymer extensively used in biomedical application and are nontoxic and highly biocompatible. The process is simple and can be carried out in room temperature without using any expensive or complicated instruments and refrigeration. In experimental animal wound models, the polylactide membranes showed faster wound closure with increased strength of the healed skin over currently used polylactide composite membrane. Once proven in animal/human model, this is expected to provide a cheap way of producing artificial skin for burn and wound treatment. NII team has bagged the Second prize at Intel-UC Berkeley Technology Entrepreneurship award in Nov.2008 in U.S.A for the innovation (www.nii.res.in/).

4.6. S.W.O.T of the Bio-Pharma industry

Strength

Potentially a huge market

The sector analysis in the previous section clearly indicates a great potential in the Bio-Pharma market. If the new gelatin based product goes through the clinical stages successfully then tapping this market would definitely mean year on year profits.

Weakness

Low per-capita expenditure

A study by the Indian Commission on Health in India (2009) indicated that 56% of Indian health expenditure is on drugs, equivalent to around US$17.9 billion in 2004, but much of this is on traditional Indian remedies rather than allopathic drugs. A large proportion of pharmaceutical expenditure is tax, which is equivalent to around 30-35% of the total according to the OPPI, taking into account customs duty, excise, sales and other taxes.

Concerns remain that the presence of fakes or substandard medicines in India is alarmingly high. Despite the efforts of large companies to protect their products, such as the use of holograms, counterfeit drugs remain a problem. The market for these drugs is estimated to be as high as 15-20% of India's total pharmaceutical market (Espicom, 2009).

Problems with some contract research organisations not adhering to international GCP/ GLP standards when undertaking bioequivalence studies (discussed in sec 4.4)

Opportunities

Mergers

Mergers provide opportunities such as entering new markets, expand the group's core capabilities, enhance market share and bring new products under the group's product portfolio which could enables strong growth prospects for the new skin regenerative product. International companies are showing great interest in entering India via alliance with Indian Pharma companies.

GSK announces a strategic alliance with Dr. Reddy's Laboratories Ltd - GlaxoSmithKline plc (GSK) has announced an agreement with Dr. Reddy's Laboratories Ltd (Dr.Reddy's) to develop and market selected products across an extensive number of emerging markets, excluding India. This is another significant step forward in strategy to grow and diversify GSK's business in emerging markets. Growth in both population and economic prosperity is leading to increased demand for branded pharmaceuticals. This new alliance will combine Dr. Reddy's portfolio of quality branded pharmaceuticals together with GSK's extensive sales and marketing capabilities (Pharmaceutical Business Review, 2009).

Perfect competition among Collagen based products

As mentioned in the previous sections the products that are currently there in the market for skin regeneration are all collagen based products. These products are very expensive and thus there is a price war among these products. Any new product in the market which performs similar tasks and activities and at much affordable price could have a superior advantage in the Wound and Skin care management industry. There could be a potential First Mover Advantage for that product.

Government Initiatives

The Karnataka government announced its plan for a revised Millennium Biotech Policy at the Bangalore Bio 2009 by Karnataka Chief Minister, B S Yeddyurappa. The revamped biotech policy aims at bridging academia with the industry. The State government is committed to providing an industry-friendly and business-friendly environment for the growth and development of knowledge-based industries.

Another initiative of the government is to develop a biotech cluster in Bangalore, which is phase-II of the expansion of the biotech park in Electronic city on Hosur road. The project, to be built on a public-private partnership model, will involve Rs 300 crore investment. The state will contribute 60 acres worth Rs 100 crore and the remaining investment is expected to come from private players.

The state government commissioned a Rs 16 crore R&D and institutional block comprising of IBAB (Institute of Bioinformatics & Applied Biotechnology) and CHG (Centre for Human Genetics) at the biotech park in February, 2009. The government of India, recognising IBAB as a centre of excellence, has given approval for setting up the Rs 34 crore Bio-IT centre there.

Threat

Regulations related to animal-derived products:

Certain products such as dermal regeneration products, biomaterial products for the spine, nerve and tendon repair products among others, contain materials derived from animal sources, are increasingly subject to scrutiny in the media and by regulatory authorities. This public scrutiny has been particularly acute in Japan and Western Europe with respect to products derived from animal sources, because of concern that materials infected with the agent that causes bovine spongiform encephalopathy, otherwise known as **BSE** or **mad cow disease**, may, if ingested or implanted, cause a variant of the human Creutzfeldt-Jakob Disease, an ultimately fatal disease with no known cure.

Certain countries, such as China, Taiwan and Argentina, have issued regulations that require its collagen products be processed from bovine tendon sourced from countries where no cases of BSE have occurred. Similarly, the EU has requested that its dural replacement products be sourced from bovine tendon sourced from a country where no cases of BSE have occurred or classified by European Standards as Class IV material (Integra Live Science Cooperation, 2007). In addition, among other regulations, Japan requires that the tendon used in the

manufacture of medical devices sold in Japan originate in a country that has never had a case of BSE.

Currently, companies like Integra purchases its tendon from the US and New Zealand (Cetification Requirements USDA, 2008). If Integra cannot continue to use or qualify a source of tendon from New Zealand or another country that has never had a case of BSE, the company will not be permitted to sell its collagen haemostatic agents and products for oral surgery in many countries. Ban of such products, could have a material adverse effect on any company's business.

Chapter 5: Product Analysis

As a part of the science bridge initiative, the skin regenerative graft that is being developed for addressing not just burns (second or third degree burn) and wound injuries but also to treat diabetic ulcers (deep wounds). This tissue engineered product is particularly designed to handle complications that arise from autograft treatment (traditional procedure) and with the aim to be economically affordable by majority of people in developing countries. The information articulated in this chapter is mainly from the data gathered during interviews and field visits.

5.1. Current Situation

Collagen is a protein that is derived from Bovine (animal sources). This helps the dermal cells to grow during skin regeneration. The scaffold used currently in the market come with the combination of antibodies and thus as a single layer. Silver is commonly used as an antibody. These scaffolds come with a coating of fibrinogen (Bio active molecule) that assists the development of blood vessels and not just the dermal cells.

Despite the high percentage usage of these kinds of products in the UK market as well as Indian market, there are a couple technical drawbacks that are equally accepted among patients and doctors.

> *"*These products take a lot of time for healing. The regeneration is very slow as there is no 100% protection offered to prevent infection Therefore the fibroblasts develop into the next state which is the miofibroblasts, which appears as a shiny surface...*"* says Dr Ashok Kumar

The slow regeneration is due to the infection which in turn is due to the shortage of antibacterial agent. To further elaborate, an ideal scaffold for this purpose should have very good degradable properties. Collagen, which is the main ingredient of the scaffold acts as a good degradable substance that is best suited for the purpose. However, most of the collagen products in the market are mixed with the antibacterial agent (mostly silver) to form a single layer. Therefore the degradation of both the substances happens in parallel exposing the wound to infection. This technical drawback results in the development of a scar post treatment.

Secondly, it is important that the scaffolds have good absorption capacity as the wounds have lot of exudes. The burn surgeons who were interviewed in Bangalore believe that having a good absorption capacity is a vital characteristic in such products. They also said that most of these internationally available products are not very popular in India mainly because of the cost factor.

> *"These products are way too expensive to be bought by patients visiting the government hospitals"* says Dr. Vasunetra, Bangalore Medical College.

And when the surgeons from the private hospitals were interviewed, they had similar answers that pointed out to the heavy pricing of the product. It is evident by looking at the burns statistics in India (appendix) and the UK (appendix) that the demand for products to treat 2nd and 3rd degree burns and wounds is increasing.

5.2. The Process

Based on the qualitative research done by interviewing Burns department surgeons in Bangalore, Nottingham and Sheffield the process followed currently in India and UK for treating burns and wound are discussed below.

Victoria Nursing Home, Bangalore (Specialty burns center government hospital):

Burns on a patient are first classified as less than 20% or greater than 20% depending on the location of the burn on the body. The later is an elaborate process involving IV fluids which are injected into the patient's body to regain the lost body fluids. After the burn, for the next 3 to 4 days the patient is treated with various antibiotics and painkillers. An ointment (Neosporin) is used if the area of burn is facial and drugs like Deriphylline, Hydrocortisone and Budacort Nebulization are used in case of respiratory burns. Finally, around day 4/6 a dressing using either Kollagen or calgigraft is done.

However if the burns are less than 20% the patient is treated with just ointment of Silver Sulfadiozine and anitibiotics like ciptofloxocine and painkillers are prescribed.

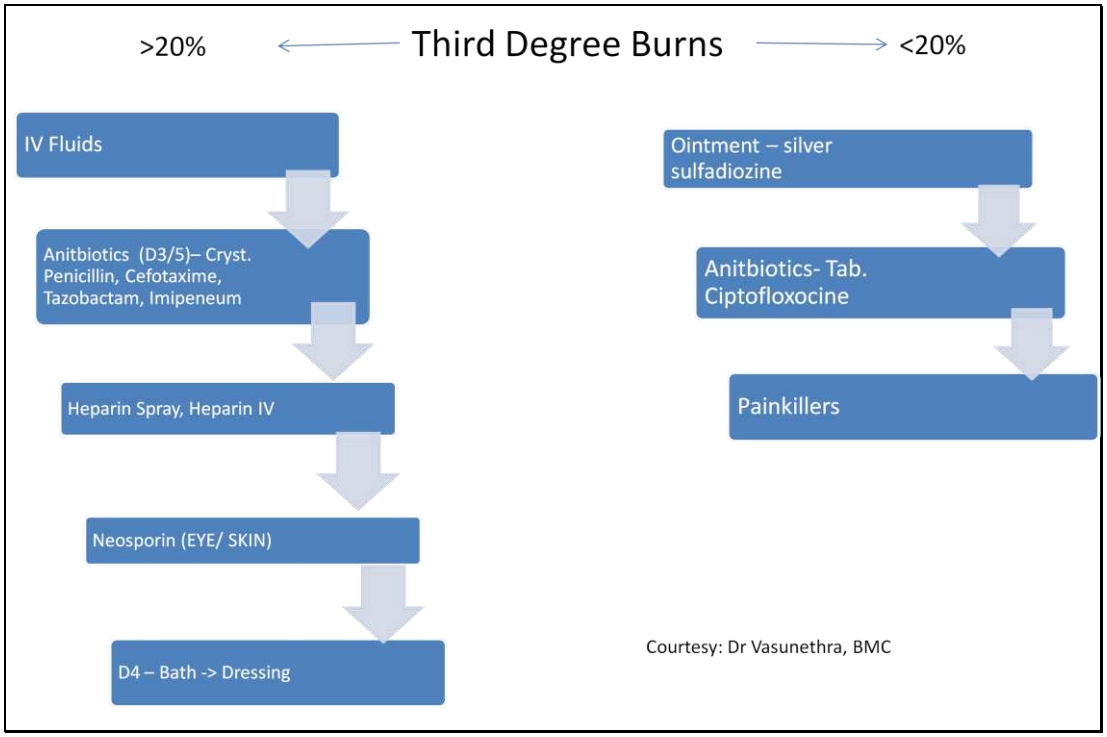

Figure 22: Process followed in treating 2nd and 3rd burns in Vitoria Nursing Home, Bangalore

Clinical Sequence for treating wounds:

It was found that majority of the hospitals in India followed the above procedure to treat burns/wounds. Among the commercially available products, the most commonly used product in India is Kollagen and the next most popular product is Hellicol. However, in the US, UK and other European countries advance dermal regeneration products are being used to treat burns and wounds. The clinical process of treatment using these products would approximately take 30 days for wound closure. In approximately 14 to 21 days, the scaffold is eventually remodeled as the patient's cells rebuild the damaged site. Complete wound closure occurs as epidermal cells migrate from the wound edges. The clinical sequence for treating wound is presented in the below flow chart. For large wound, a layer of epidermis may be applied to the wound area to facilitate complete wound closure.

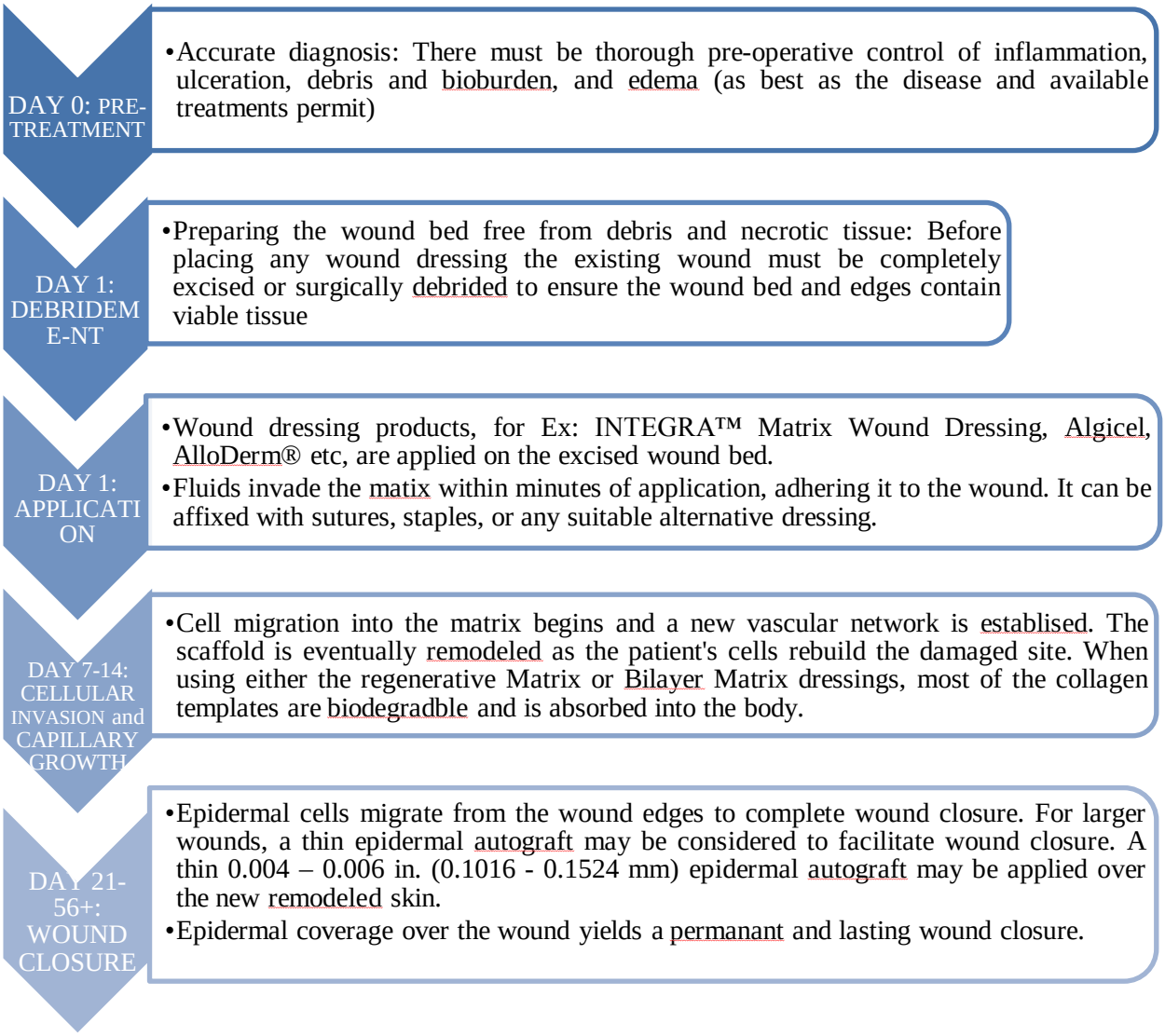

Figure 23: Clinical sequence for treating burns or wounds using regenerative skin grafts

5.3. The working environment

As the science of wound care advances, the new product developed in the labs of IIT Kanpur biosciences department provides caregivers with alternatives that deliver wound dressings offering superior performance at very lower cost. These dressings are a new and unique line of dressings. These dressings can be thought of as "all-in-one' dressings for effective wound bed preparation.

The new 'cryogel sheet' - skin regenerating graft dressings is a bi-layered dressing with a combination of a degenerative layer which comes in contact with the wound and an antibacterial layer. The bottom layer is similar to Integra, however the scaffold here is made of gelatin derived from fish source.

> "Collagen is a polymeric chain and gelatin is the hydrolyzed part of the chain. This material made of similar amino acids that recognizes the cells. Also, gelatin is almost 10 times less expensive than collagen" – Dr Ashok Kumar.

Therefore the new product promises cost effective product with high acceptability in the market. The unique multilayer design provides a wound dressing that is easy to apply with high degree of flexibility in terms of application.

Regenerating template

The Regenerative Layer is the bottom layer which comes in contact with the wound and is brittle by nature when unpacked. However, before its application on the burn/wound, it is dipped in water. This changes the properties of the material and makes it strong and flexible. The main composition of this material is gelatin and fibrinogen (for angiogenesis[8]). This dressing is designed for placing directly on the wound. The dressing can be left in place for up to 3 weeks depending on the amount of burn/wound drainage. This layer dressing is composed of specially formulated cryogel sheets that are extremely flexible, minimally adhering and delivers superior absorption capabilities (capillary action). This Cryogelation technology is patented to IIT Kanpur. The cryogel sheet has a smooth bottom surface (which comes in contact with the wound) and the upper rough surface. The antimicrobial layer will be placed on this layer and it is 100% covered, uniformly and circumferentially approximately with a thickness of 2mm thickness.

This dressing is extremely versatile and user friendly, they seem to conform to hard-to-dress areas and providing mild compression when needed. Wound Contact Dressing are indicated for management of incisions, skin grafts, donor sites, lacerations, abrasions, pressure sores, chronic wounds, chronic ulcers, dermal ulcers, vascular ulcers, and diabetic ulcers. These dressings can be thought of as "all-in-one' dressings for effective wound bed preparation.

Key Characteristics:

- Provides immediate wound coverage

[8] The process of creation of blood vessels

- Highly conformable for various anatomical sites
- Excellent performance in deep donor sites as it can be applied as multiple layers.
- Exceptional strength and flexibility
- Room temperature storage
- Long shelf life
- Can be used separately without the dressing template covering it.

Dressing template – Antimicrobial layer

The top layer provides a topical antimicrobial barrier that reduces the bacteria and fungi counts on the wound surface and within 2 to 4 millimeters of the wound surface and also from the external environment. The dressing material is made of Polyvinyl pyrolidone (PVP) cross linked with polyethylene glycol diacrylate (PEG – Da). Lab experiments has shown to have powerful and long-lasting antimicrobial activity.

> *"The rate* of diffusion into the regenerative template would go on for minimum 2 months period.." says Dr. Ashok kumar

The biocompatible PVP releases the antibodies (Iodine) in a controlled manner- similar to that of ionic silver (used by few products in the market in this segment) - but without the associated toxicity of ionic silver. PVP exists as a liquid form however, IIT Kanpur have developed a procedure to make it into a "non-degenerative sheet" format of varied dimensions.

Key Characteristics:

- Has very high tear strength
- Could be used separately as a dressing material
- Controls water vapour loss
- Long shelf life (2 years) and can be stored under room temperature

Going that extra mile

There is a parallel research that is being carried out in IIT Kanpur where the focus is on developing a product with *'wound aesthetic look'*. After three weeks of regeneration of the dermis skin the team is working on putting a layer of keratinocytes[9] on the top of the newly developed dermis by removing the dressing covering this layer. The keratinocyte layer is a tissue cultured cell sheet which is cyopreserved (Low temperature preservations) in the hospitals. They claim that this would result in regeneration of original skin!

> *"These stem cells would increase the costs by 20-30 folds"* says Dr Ashok kumar

Since this procedure involves high costs the target market is mainly the developed countries like U.S and UK.

[9] Keratinocytes are stratified, squamous, epithelial cells that comprise skin and mucosa (AAD, 2009)

5.4. Operational Plan

Raw-materials

The current operational environment is only under lab conditions. Therefore the raw material requirement and usage is scaled down to a great extent when compare to the mass scale production in the factories. For the regenerative layer the raw-material used is just gelatin derived from Piscean source. For the dressing material the rawmaterials used are Iodine, Polyvinyl pyrolidone (PVP), and polyethylene glycol diacrylate (PEG – Da).

Suppliers

Irrespective of the lab environment or at a commercial scale, a typical supplier for manufacturing of this kind of product would be a Life Science and High Technology company whose biochemical and organic chemical suppliers cater to the scientific and genomic research, biotechnology, pharmaceutical development, the diagnosis of disease and chemical manufacturing. In the labs of IIT Kanpur, the rawmaterials are procured from one such leading life science supplier called Sigma-Aldrich.

Address: Plot # 12, Bommasandra Jigani Link Road, Bangalore - 560 100
Phone: +91-80-6621 9400
Fax: +91-80-6621 9450
email:india@sial.com
Web: http://www.sigmaaldrich.com

An Ethylene Oxide Sterilizers and a cryostat are the main machinery needed for the manufacturing of this product. The supplies for sterilizers could be firms like Kaustubh Enterprises, Rujikon (www.indiamart.com/kaustubh/) and for cryostats it could be companies like Sipcon Instruments Industries (www.sipconinstrument.com/cryostat.html).

Manufacturing:

Since the technology involved in the manufacturing of these materials is very simple, the cost involved in setting up the machinery is low. The patented manufacturing technique followed for producing the regenerative template is called Cryogelation technique. The dry solid sheet of gelatin is sterilized by using Ethylene Oxide Sterilize. For manufacturing the dressing material, the cryostat is used. A special technique that is unique to IIT Kanpur is adopted to convert the liquid raw materials into solid sheets of 2mm thickness that could be later placed over the wound/burn as a dressing.

Packaging:

The product would be available in the market in three different probable formats. The regenerative template and the dressing template would be available separately in two different packages; alternatively they would also be available packaged as one unit. The regenerative template will be dry and sterilized before packing. The dressing template is also

dry during packaging, however it is not sterilized. Both the templates could be stored in dry temperature with a very long shelf life.

5.5. Financial Information

The impact of Budget 2009-10 on Bio-pharmaceutical industry has been quite positive. Custom duty on Advance Medical Equipment has been reduced, so the cost of new advanced plant in the research and manufacturing sector will come down. The 150% of weighted deduction on in-house research has been for all the manufacturing business being extended except for a small negative list. In the budget, Rs20.57 billion is allocated for healthcare sector to strengthen the PHC and to increase the operation of 24×7 facilities.

Despite the positives there are few negative effects as well: central excise duty has been increased from 4% to 8%, which will reduce the margins of the manufactures. Even Minimum Alternative Tax (MAT) has been increased from 10% to 15% and has increased from seven to 10 years (Ministry of Finance - Govt. of India, 2009). The budget seems like the excise duty cut and other proposals may help the common person but not the company.

In spite of the early stages of the new product life cycle, a cost estimate was done by considering the industry standard cost structure as the benchmark. The figure below gives a breakdown of various parameters that contribute of the final pricing of the bio-pharma product.

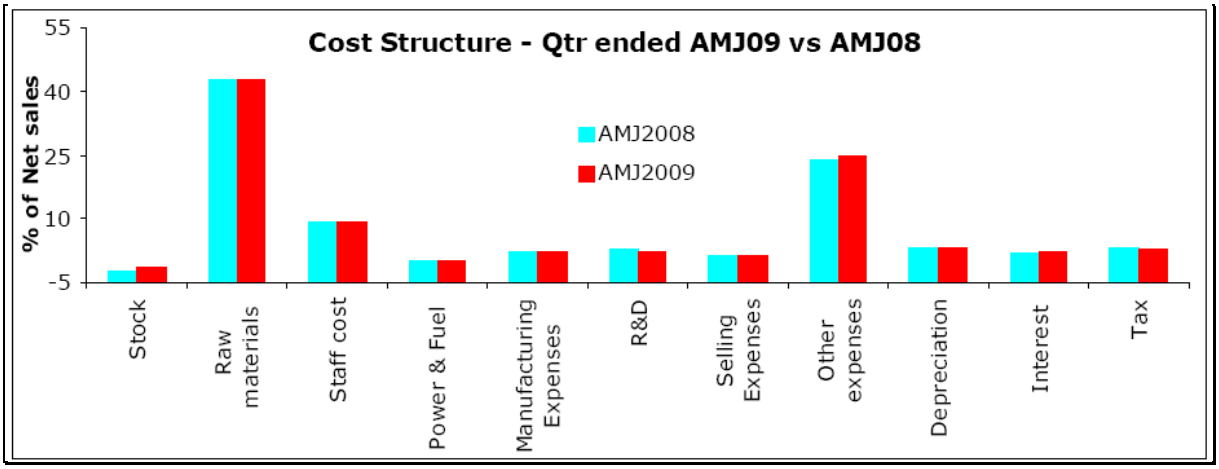

Figure 24: Cost Structure as percentage of net sales. Source: BSE India, Cygnus Research

Cost Structure as Percentage of Net Sales AMJ 08 Vs AMJ 09										
Company	Ranbaxy		Dr Reddy		Cipla		Piramal		Industry	
Year	09	08	09	08	09	08	09	08	09	08
Stock in trade	-1.67	-8.14	-1.37	-0.12	-1.05	-3.61	2.05	-1.70	-1.12	-2.24
Raw materials	42.56	41.27	35.91	36.20	47.19	46.69	40.24	37.50	42.84	42.85
Staff cost	9.00	10.20	9.85	9.85	6.50	7.00	11.85	12.93	9.13	9.36
Power	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.17
Manufacturing	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.54	2.46
R&D	9.35	8.71	8.52	7.78	0.00	0.00	4.15	1.82	2.12	2.70
Selling Cost	0.00	0.00	9.98	9.85	0.00	0.00	0.00	0.00	1.29	1.33
Other expenses	70.74	42.07	11.73	12.33	25.52	30.13	26.31	31.17	24.87	23.99
Depreciation	2.56	2.40	3.01	4.17	4.22	3.17	4.16	3.97	3.20	3.35
Interest	2.13	2.60	0.45	0.15	0.84	0.30	0.92	0.84	2.31	1.95
Tax	0.42	-0.37	2.80	3.64	2.87	2.53	1.08	1.37	2.75	3.25
Source: BSE India; Cygnus Research										

Table 6: Comparative cost structure between 2008 and 2009 . Source: Cygnus Research

5.5.1. Extrapolation from the financial data

To extrapolate the approximate price of the product in the make, firstly, the costs were noted. The machine costs are only one time investment. Besides, if it is a well established Pharmaceutical/biotechnology company then these costs could be canceled. The reason being, sterilizers and cryostats are widely used in such companies for other purposes.

Cost of Cryostat – approx Rs. 3,00,000 (www.sipconinstrument.com/cryostat.html)
Cost of sterilizer – approx Rs. 5,00,000 (www.indiamart.com/kaustubh/)
The above costs of equipment is only for small scale manufacturing (in the lab condition)

Cost of Raw material used:
Gelatin from fish skin – 500gm costs Rs 2,780 (product #G7041-500G from www.sigmaaldrich.com)
In comparison, Collagen from bovine Achilles tendon – 25gm costs Rs 19,100 (product #C9897-25G from www.sigmaaldrich.com)
Similarly, form the same firm, Iodine of 100gm costs around Rs 610, PVP of 1 Kg costs around Rs. 3000 and PEG of 500ml costs Rs. 5000.

Calculations:

a) Regenerative Template
2gms of gelatin is required to produce a 10X10 cm sheet of regenerative graft (IIT Kanpur Research Team).

Therefore for 500gms – 250 sheets – approx Rs.3000
For 1 sheet it would cost 3000/250 = **Rs 12/sheet** (Raw material costs only)

b) Dressing Template
For 2000 sheets of 10X10 the raw material required are
Iodine (100gm) Rs 610 + PVP (1Kg) Rs 3000 + PEG (500ml) Rs 5000 = Rs 8610 (IIT Kanpur Research Team).

Therefore for 1 sheet the cost would be 8610/2000 = **Rs 4.3/sheet**

The total cost of a 10X10 cm sheet of regenerative layer and the dressing template would cost 12 + 4.3 = 16.3 ~ **Rs. 17**

By taking the data in the previous section on cost structure as a percentage of sales, the multiplying factor could be found out. If 42.84% is the industry standard for percentage of raw material, then the derived multiplying factor is 0.396. By using this value the remaining parameter that account to the final price of the product can be extrapolated. For ex: 'Other expenses' would account to 0.396 X 24.87 = Rs. 9.84

Similarly, after calculating the costs for all the other parameters, the summation of these costs would account to the final price of a 10 X 10cm (or *5′* X *5*) size regenerative template as well as the dressing material. Therefore, after all calculations the total price of this gelatin based product would be around **Rs. 38** (including tax)**.** For a **box of 10 sheets** it would cost around **Rs. 400** only! (or $10)

5.5.2. Pricing Power

The products in the market for wound management like the skin regenerating graft are ideally packaged in either a box of 5 or 10. The size of one sheet varies from company to company. The price breakdown of few competitors products are mentioned in the table below. To ease the comparison, the cost of the product for a dimension of 5" X 5" or 10cm X 10cm is also mentioned. It is very clear by the comparison that the new product is extremely cost effective and could very well have a monopoly in the sector.

Product Name	**Pricing**	**Source**
Promogran™ Matrix Dressing (Johnson & Johnson)	4.3" x 4.3" is $17. Therefore a 5" x 5" would cost around **$22**	www.allegromedical.com
ADAPTIC Non-adhering Dressing (Johnson & Johnson)	3" X 3" is $2.15. Therefore, a 5" X 5" would be around **$5**	www.allegromedical.com
Aquacel® Hydrofiber® Pad	4" X 4" 10/Box costs $138.46. So, , a 5" X 5" would be around **$21**	www.betterlivingnow.com
Biobrane® Biosynthetic wound dressing	5/Box pad EA 5" X 5" costs $319.50. Therefore one 5" X 5" sheet is **$32**	www.betterlivingnow.com
Cellerate RX™ Activated Collagen Gel	1 each (28 gm) is $63	www.betterlivingnow.com

Chapter 6: Discussion

The global Biotechnology market clearly indicates that it is very lucrative as it contributes to the generation of 21.27% of world's Phrama revenues. China and India have emerged in the top 5 markets growing big and fast. Furthermore, the Bio-Pharma industry accounts to almost 75.24% of the biotech industry making it the most attractive market to carry out R & D. India has become an hot destination by attracting foreign investment companies and MNCs (Appendix A) to set up facilities and joint ventures. The shift toward research driven market is getting its momentum from the large inflow of foreign funds (100% FDI investment allowed – section 4.3.2). The government of India has taken the initiative to restructure the regulatory policies in order to assist R & D and manufacturing industries. These market conditions make it ideal for companies and research institutes to invest time and effort in this sector.

In the global wound management market segment has a lot of potential in the China, UK and India. The Chinese Biotechnology industry is leading in terms of revenue generation. UK market has shown great potential for growth and accounts 2nd in the overall Biotechnology revenue generation in whole of Europe. However in UK the pricing of the product would have less impact as the nation displays very low price sensitivity as the state run health services (NHS) will aim to keep their spending low. The new wound management product made by cyogel sheets would have a very high demand in UK as it has the properties of Hydrocolloids (account to 33.8% of market share) and Hydrogel sheets (account to 10.6% of the UK product market share). Also, the burn statistics has worsened YoY (Appendix D). In Nottingham alone the 3rd degree burns accounted to 25% of the burns in 2007 which increased to 28% in 2008. Among all the burn cases in Nottingham city, 40% account to 2nd degree burns (Appendix E).

The DBT in India is the backbone for Biotechnology as it accounts for policy making, promotions of R&D, international co-operation and manufacturing activities. The institutional framework and the funding opportunities are enormous unlike in other developing countries. The history of Venture capital investors further reinstates the argument. Government initiatives like the National Biotech Development Strategy that lay a roadmap for the next 10 year in the field of Regenerative Medicine and Bioengineering is encouraging for acadamia and companies to carry out research work and launch products with cutting edge technologies. Once the new skin regenerative product goes through all the clinical trials successfully, it should be in a good position to tap that 80% of unmet demand for wound care in India (section 4.3.3).

6.1. Literature review and empirical evidence

In the previous chapter, it was discussed that it is important for the product to be of good quality rather than reaching the market the quickest. It was found that the team in IIT has this as their motto and is focused on extensive research on regenerative template and the dressing material. Cryogellation, which is a part of Cell encapsulation techniques (discussed in section 2.3) is used in developing this template. An extensive backward roadmapping was done to

understand the demand for the skin regenerative products in India. The price oriented population was the target. The technology push happening at the moment is a Cryogelation technology where the process is patented to IIT, Kanpur. This techniques helps in creating a gelatin based skin regenerative template with good interconnectivity between the pores and thereby making it a very good medium for the cells to be absorbed and then multiply.

The tests conducted at the moment are only laboratory based. Initial tests have already proved that the new product has a very good absorption capacity; extent of natural tissue replacement is phenomenal with the ability to retain differentiated cells. The tests have also shown the ability of the new product to retain its shape after implantation in the host. Animal testing would be the next step followed by the clinical trials. This indicates that the product is very much in the preclinical phase of its life cycle. Although the product is very promising, the only disadvantage is that it would take a minimum of 5 years before it reaches the market. The results of clinical trials phase would be crucial in determining the technology pull.

It was observed, while interviewing various surgeons in India, that lack of awareness of the product's characteristics played an important role in creating the demand for the product. Most of the Indian products like Hellicol were not used in Victoria Hospital only because the surgeons were not aware of the advantages of using it instead of a plain collagen sheet. To prevent such problems, the new regenerating graft must look at making technical flow of information in parallel to the order information. Since it is one of the kind, it would be even more important to inform physicians and surgeons about the usage.

There are no skin regeneration products in the market which are made of gelatin. This main difference alone is a strong point for product differentiation that was discussed as essential (in the literature review section) for pricing it either high or low. Based on analysis of other products, the competitive response is likely to be very low for many years to come. Therefore, a company owning this product has the liberty of pricing the new skin regenerative product over a broad range of pricing.

A rough business forecast on the pricing was done based on the market analysis and industry standard. The price of the new Skin regenerative product is indeed competitive. However, in reality there are several other aspects that need to be considered. The accuracy depends on how the technical and manufacturing personal on the product development team assesses per-unit costs. The difference between the revenue and cost of goods sold is the gross margin available to cover fixed costs and contribute to profits. Although the price of the new product is estimated around Rs. 40 for a 10 x10 cm sheet, a company owning the product could increase the price further up, but still lower than the competitor's pricing, and have huge positive difference in revenues and cost of goods. This would in turn contribute to huge profits for the company.

The costs incurred for R & D and concept testing, as well as anticipated costs for prototype development, equipment and materials, labor, product testing, and additional market research would all attribute to the development costs. Since the product has to go through clinical trials, it would involve additional capital expenditure. Once the clinical trials are successful,

marketing costs start at the prelaunch. These would include advertising, distribution, sales promotion, sales force coverage, miscellaneous selling and communication costs. An overhead will also have to be allocated for administrative costs. Regardless of the company's attitude toward cost allocation, it is imperative that the estimated revenue (either price or number of units) is not artificially inflated simply to cover these costs. The amount that finally remains after subtracting the development costs, marketing costs and the overhead costs is the gross profit. This is where the product is expected to contribute to indirect fixed costs, taxes and profit. In this case, it appears to have a potential for huge profits.

6.2. External factors in decision-making

Approval from Drug Control General of India is essential for initiation of clinical trials:

For approval purposes, clinical trials can be classified as (Pharmabiz, 2009)

- Category A: In this category the approval time is around 2-4 weeks and it includes clinical trials whose protocols have been approved by USA, UK, Switzerland, Australia, Canada, Germany, South Africa, Japan or the EMEA.
- Category B: The regulatory turnaround time in this category would be around 8-12 weeks. It includes clinical trial protocols which have been approved in a country that is not listed in Category A.

Clinical research organizations (CROs) have to obtain 'no objection' letter from Drugs Controller General of India(DCGI) and import license to import the research drug. If the samples have to be exported (UK or China) then export license is required from Directorate General of Foreign Trade (DGFT). Also, Registration of trials involving humans has been made mandatory starting in June 2009 on the Clinical Trials Registry-India (CTRI) website (livemint & wall street journal, 2009)

Chapter 7: Conclusion & Recommendation

To identify the criticality of a success factor, measuring the performance of the new skin regenerative product is needed. In the biopharmaceutical R&D business, it is difficult to measure performance. In an early phase when speculating whether a product will survive and do well in the global competition as desired, there are usually no products in the market and little, if any, positive cash flow for years to come. However, some benchmarks for successful performance could be identified:

- Receiving venture capital (VC) funding
- Collaborating with a partner
- Conducting a successful initial public offering (IPO)
- Having a product candidate complete a successful clinical trial
- Finally, launching a product into the market

Again, collaborating with a partner can be both a measure of performance and a CSF. It measures performance in the sense that the partner has considered the company to be a valuable ally and the co-project to be worth the risk. Or, it can be a CSF in the sense of gaining resources and experience essential to making the project under collaboration succeed and at the same time making the company succeed. A successful IPO indicates a good company in the sense of public evaluation. At the same time it creates cash inflow important for the company. Is money a success factor? It surely is critical for the company's existence. Capital from VCs or IPOs and cash inflow from product sales are considered to be the outcome of having the 'right' success factors in the company, not merely success factors per se.

Exploring Industry Schemes: Small Business Innovation Research Initiative (SBIRI) is the first scheme initiated by the Department of Biotechnology, India in 2006-07 for encouraging the small and medium enterprises to take innovative, high risk R&D projects for establishing proof of concept as well as for development and commercialization of research leads having market demands. The proposals under the SBIRI scheme are funded in two phases i.e., Phase-I & Phase-II. Under Phase – I, risky but innovative, early stage, pre-proof-of-concept R&D at lab scale is funded; while in Phase-II, support is for validation, scale-up, process & product development and commercialization. The support from the department under the scheme does not involve cost of land & building. The funding pattern under Phase-I and Phase-II are available at www.dbtindia.nic.in . Since its inception, about 500 proposals have been received in nine batches.

Area-wise percentage is as follows:

- Health-47%,
- Agriculture-20%,
- Industrial products and processes-18%,
- Instrumentation and devices-6.5%,
- Environmental biotechnology-3.7%,

- Food & Nutritional Biotechnology,
- Bioinformatics and other areas-4.8%.

The most important point to note is that under health (47%), few early leads from SBI Projects are:

- A silk protein blend film-for burn wound management
- A homologous natural bio-material for treating cancer lesions & burn wounds

So far 48 projects have been sanctioned. During 2008-09, 12 projects were sanctioned out of 87 proposal received in two batches. SBIRI scheme has been well received. A review undertaken by IIM, Bangalore has suggested to accommodate broader range of bio-tech industries ensuring that more SME's are benefited as also nationally relevant projects could be implemented.

Further details could be obtained on url: http://dbtindia.nic.in/uniquepage.asp?ID_PK=36

Indo-UK: DBT-Welcome Trust Fellowship Scheme in Biomedical Research: Since the new bio-pharma product is in the lab phase undergoing lab tests there is a lot of scope for research activities. Indian Biotechnology department's endeavour for international cooperation and partnerships to attain global recognition, exploring mutually advantageous science collaboration and meeting international standards could be of great assistance. The Department of Biotechnology in India has partnered with Welcome Trust (WT), UK to launch a three-tier fellowship programme on biomedical research at postdoctoral level. The Welcome Trust is an independent charity funding research to improve human and animal health. The DBT and the Welcome Trust each have committed £8 million per year, for a period of ten years. The scheme is devised to support basic, clinical and veterinary research. Details of the Alliance are available at www.wellcomedbt.org.

Major factors limiting the growth of indigenous medical devices industry are the high cost and non-availability of imported technology, higher risks involved in producing and marketing medical devices, inadequate indigenous technology development and production of biomaterials and device and lack of a regulatory authority for medical devices in the country.

The research area that is currently being pursued in IIT Kanpur seems to offer excellent revenue and profit potential. However, during the path towards its launch in the market it is essential to have a closer tracking of profiles and related research programs and academe. In addition, they will also have to pay more attention to economics of drug development process. A product patent is granted for a period of 20 years. Taking a Bio-Pharma product from drug discovery stage to market takes anywhere between 7 to 10 years, leaving about 10 years for recouping investment. Besides identifying the research area (which is already done in this case), managing the drug development process is critical skills that the research institute need to acquire. Reducing time-to-market is as important as discovering new grafts as alternatives for existing expensive products. However, time-to-market is even more important for Bio-Pharma products that are new to the industry and segment like the gelatin

based product. In the generics market, market exclusivity period has assumed great importance. The first company to enter the market will get to enjoy a premium. Therefore, new product development plays even more critical role in the generics market.

The cost of producing a marketable pharmaceutical product has increased sharply in recent years due to greater regulatory control, increased competition and globalization. Now, more than ever, pharmaceutical companies must outsource research and development works to their biotechnology counterparts— and they are doing so in record numbers. Pharmaceutical companies bring to these partnerships is the ability to navigate regulations minefield and of course, marketing expertise.

Academic collaborations with industry are a win-win deal for both. Academia gets the much needed funding for research while the industry can lay its hands on breakthroughs as soon as they occur. Alliances for manufacturing can also be a beneficial for both the parties where the manufacturer will be able to concentrate on core manufacturing at a lower cost which advantage could be enjoyed by the partner company. Players who are producing in bulk (skin regenerative grafts) by tying a long term contracts through alliances could de-risk their business—resulting in a smooth revenue flow. In this case by collaborations with industry, IIT Kanpur can offer breakthrough research and insights into Wound care and burn care treatment. As major markets are highly regulated and lucrative, the quality standards are a must to enter those markets. Standards such as Good Manufacturing Practices and Good Clinical Practices will become a must in the years to come.

While numerous advances have been made in the science of biological tissue engineering in the past few decades, the ideal skin replacement remains elusive. None of the currently available products in the market fulfill all the criteria of a "perfect" skin replacement. Currently, the patient's skin remains the best alternative to replace burned tissues. The advent of the new 'all-in-one' gelatin based skin regenerative product with the aim of providing 'wound aesthetic look' will undoubtedly become an ideal skin replacement. This diligently pursued applied research skin regenerative product is on the right course to be proved as a perfect replacement sooner rather than later.

7.1 Area of future research

Technical aspects of the product:

After interviewing the team in IIT lab, the results of the lab tests done so far were positive. However, the skin regenerating graft has to undergo several other lab tests before the clinical trials.

For the PVP layer

(1) Ability to detoxify and prolong the activity of Iodine

(2) Controlled release of Iodine in skin injuries

(3) Trying to minimize the toxicity of Iodine.

For the Regenerative Gelatin Layer
(1) Studies in animal models to minimize scar formation or avascularisation
(2) Inducing nerve growth and
(3) Effectiveness of gelatin on humans
(4) Hair regeneration using stem cells

Business aspects of the product:

Understanding the operational and marketing challenges faced by the Skin Regeneration grafts that are currently popular in India. For ex: Hellicoll.

Exploring the reasons for long delays in the clinical trials in India and how to overcome them?

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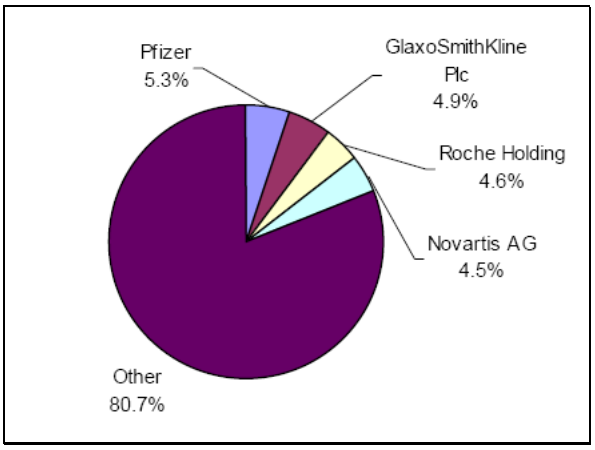
Appendix



Source: Datamonitor 2008, Global Pharmaceuticals, Biotechnology & Life Sciences
Appendix A: Industry Group Share: % Share, by Value, 2008

Distribution of Medically Certified Burn Deaths by Age and Sex in Delhi
(1991 to 2002, 2004 and 2005)

Year	Below 14 Years		15-24 Years		25-44 Years		45-64 Years		65 & Above		Total	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
1991	93	82	166	385	249	492	59	54	13	24	580	1037
1992	81	99	18	324	197	337	48	48	18	30	462	838
1993	81	98	130	400	258	396	50	54	17	27	236	975
1994	94	111	131	415	279	464	46	58	24	25	574	1073
1995	77	104	156	404	298	376	59	69	17	32	607	985
1996	4	6	20	44	38	71	8	8	8	7	78	136
1997	8	16	25	55	50	92	16	25	27	27	126	215
1998	28	30	39	164	105	190	22	13	18	13	212	410
1999	23	30	61	141	128	165	20	19	6	5	238	360
2000	12	11	11	39	21	47	7	7	258	318	309	422
2001	81	85	119	224	191	334	47	45	45	58	483	766
2002	27	33	57	100	84	132	28	24	32	58	228	347
2004	44	37	69	158	122	155	33	18	4	4	272	372
2005	76	65	104	207	177	229	73	60	31	42	461	603

Appendix B: Burn Deaths by age and sex in Delhi. Source : Directorate of Economics and Statistics, Govt. of Delhi.

Cause/State/Sex-wise Medically Certified Deaths by Diseases of Skin and Subcutaneous Tissue in India - Part I
(1997)

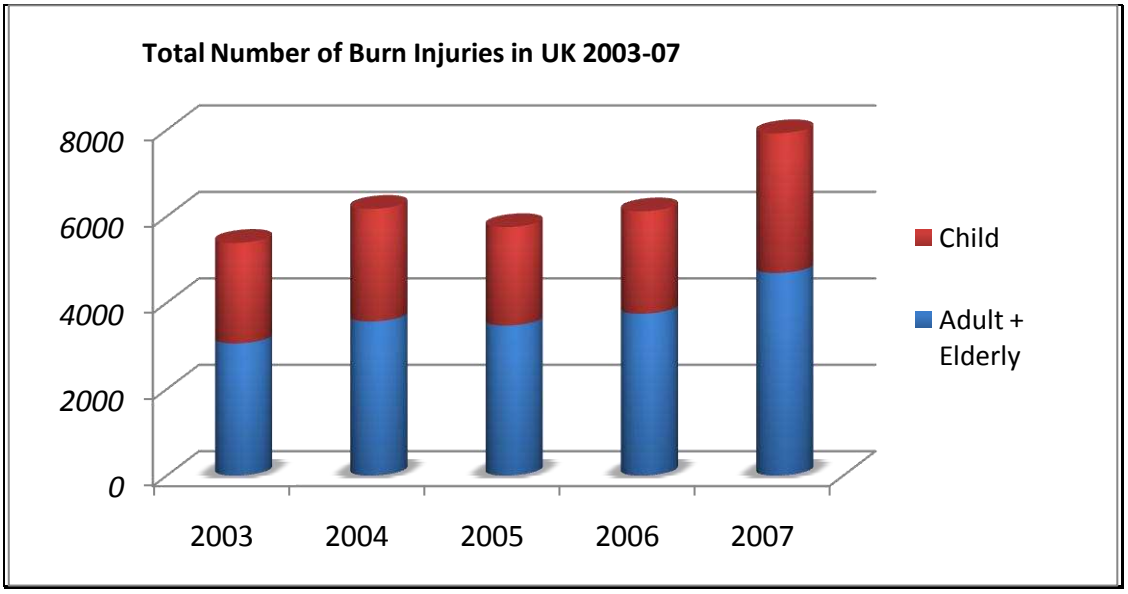
M.G./ CAT/ SC	Cause of Death	Sex	India	Andhra Pradesh	Goa	Har-yana	Himachal Pradesh	Karna-taka	Kerala	Madhya Pradesh	Maha-rashtra	Mani-pur
XII	Diseases of the Skin and Subcutaneous Tissue (680-709)	M	457	8	0	14	0	107	10	37	116	0
		F	303	6	1	1	0	42	6	15	121	3
	Diseases of Skin and Subcutaneous Tissue (680-709)	M	457	8	0	14	0	107	10	37	116	0
		F	303	6	1	1	0	42	6	15	121	3

1	Infections of Skin and Subcutaneous tissue (680-686)	M	304	6	0	9	0	79	6	37	105	0
		F	166	4	1	1	0	23	6	13	96	0
2	All other diseases of skin and subcutaneous tissue (690-709)	M	153	2	0	5	0	28	4	0	11	0
		F	137	2	0	0	0	19	0	2	25	3

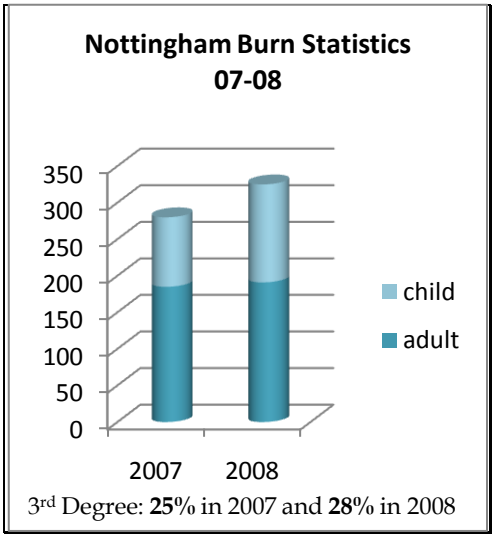
.. contd

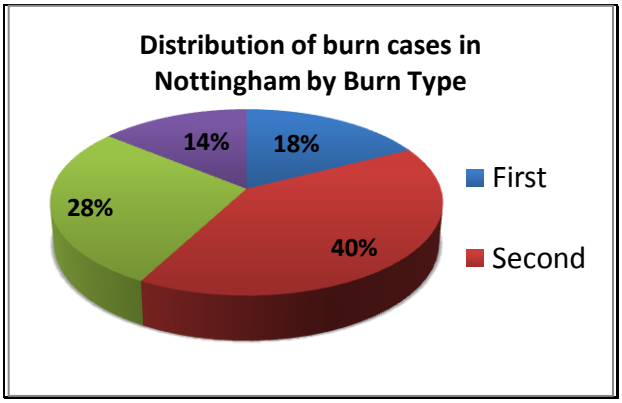
Cause/State/Sex-wise Medically Certified Deaths by Diseases of Skin and Subcutaneous Tissue in India - Part II (1997)													
M.G./ CAT/ SC	**Cause of Death**	**Sex**	**Megha-laya**	**Naga-land**	**Orissa**	**Pun-jab**	**Rajas-than**	**Tamil Nadu**	**Tri-pura**	**Uttar Pradesh**	**Andaman & Nicobar Islands**	**Delhi**	**Pondi-cherry**
XII	**Diseases of the Skin and Subcutaneous Tissue (680-709)**	**M**	**0**	**0**	**26**	**6**	**8**	**98**	**0**	**5**	**0**	**22**	**0**
		F	**0**	**0**	**9**	**3**	**0**	**82**	**0**	**3**	**0**	**10**	**1**
	Diseases of Skin and Subcutaneous Tissue (680-709)	**M**	**0**	**0**	**26**	**6**	**8**	**98**	**0**	**5**	**0**	**22**	**0**
		F	**0**	**0**	**9**	**3**	**0**	**82**	**0**	**3**	**0**	**10**	**1**
1	Infections of Skin and Subcutaneous tissue (680-686)	M	0	0	24	4	6	2	0	4	0	22	0
		F	0	0	8	0	0	3	0	2	0	9	0
2	All other diseases of skin and subcutaneous tissue (690-709)	M	0	0	2	2	2	96	0	1	0	0	0
		F	0	0	1	3	0	79	0	1	0	1	1

Appendix C: National List for Tabulation of Mortality and Morbidity
Leading Causes of Death
Source : Medical Certification of Cause of Death 1997, Ministry of Home Affairs.



Appendix D: Total number of burn injuries in UK. Source: International Burn Injuries Database, 2007





Appendix E: Burns Statistics in Nottingham Source: NHS, Nottingham

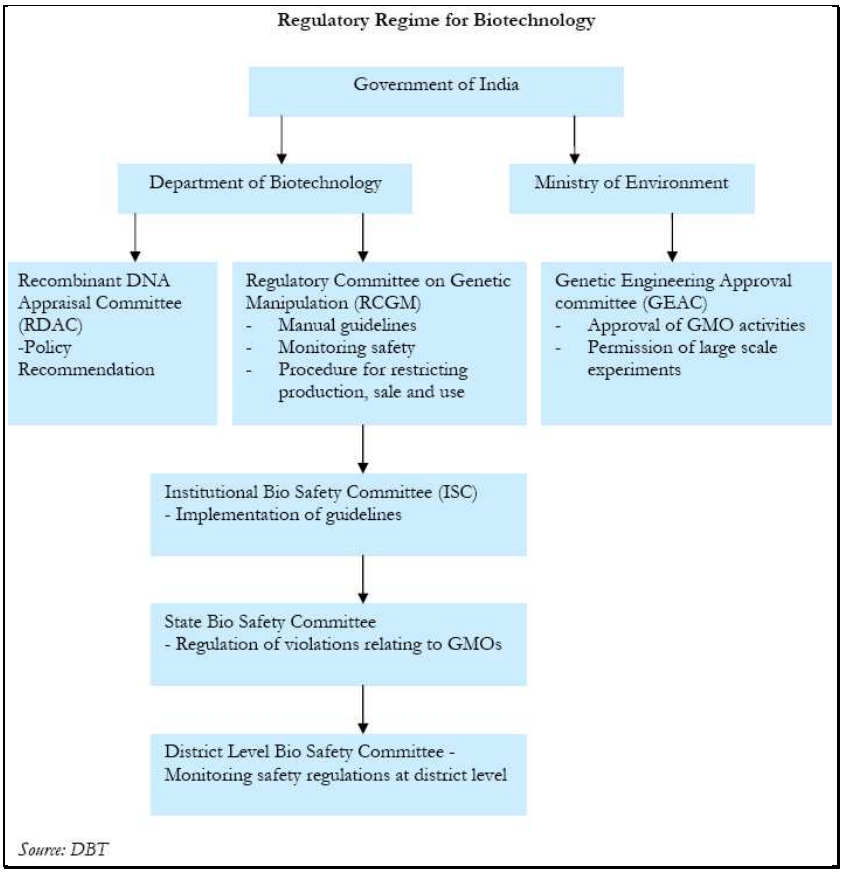
Top Therapeutic segment in India (MAT Dec)			
Therapeutic segment	2007	2008	Growth(%)
Anti-infectives	4933	6109.57	11.45
Cardiac	2741	3799.21	14.26
Gastro Intestinal	3016	3648.92	6.91
Respiratory	2545	3005.39	7.41
Pain / Analgesics	2556	2990.28	8.07
Vitamins / Minerals	2367	2677.99	3.48
Gynecology	1473	1969.7	13.07
Neuro / CNS	1471	1856.49	9.08
Dermatology	1504	1838.5	7.58
Anti Diabetic	1204	1787.19	17.73
Source: ORG IMS; Cygnus Research			

Appendix F: Top Therapeutic segment in India

Appendix G: There are six regulatory bodies in India, of which one or more deal with many of aspects of biotechnology in the country. They are

- Department of Biotechnology, Ministry of Science and Technology - which is the administrative body of regulatory approvals for investment and technology activities in the sector.
- Drug Controller General of India, Ministry of Health - which is the official regulatory body governing manufacture and commercial release of pharmaceutical products, including recombinant products.
- Genetic Engineering Approvals Committee, Ministry of Environment and Forests – which deals with bio-safety aspects and is the regulatory authority for trials and commercial release of all GMOs.
- Ministry of Chemicals and Pharmaceuticals - which is the administrative ministry for the chemical and pharmaceutical industry and governs industrial regulation and foreign investment in these sectors (enzymes. Pharma, industrial biotech products, etc).
- Department of Animal Welfare - Ministry of Health, which deals with the protection of animal rights and use of animals for scientific research experiments.

- Department of Agriculture Research and Education, Ministry of Agriculture - which deals with all field research in agriculture crops.



Appendix H: Regulatory Regime of Biotechnology in India. Source: www.dbt.nic.ac